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STUDENT SUICIDES

BY

Sir ALAN ROOK, K.B.E., C.B., F.R.C.P.

From the Department of Human Ecology, University of Cambridge

> "On 22nd March 1676 John Abramhall, commoner and undergraduate hanged himself in his chamber. The next day his doore was broke open, he was found hanging on his beame. He was the son of the parson of Foy in Herefordshire. No reason or supposition be given why he hung himself. A temperate, sober, ingenious, man."—*Life and Times of Anthony à Wood.*

The suicide of a student, who in order to have gained his place at a university must have shown intellectual superiority, is regarded by everyone as a tragedy. It is not the number of lives that are lost, which are relatively few, but the considerable upset that the event causes in the university, the grief of the parents, the sorrow often felt by some friend who believed he might have prevented it, and lastly, and by no means least, the fact, as has been rightly remarked, that one suicide in a university is one too many.

Suicide in this country is an occurrence in which social and economic factors are known to play a considerable part; it has been shown to be more likely to affect those of higher occupational status (Sainsbury, 1955), and there are indications that intellectuals as a class are more prone than are members of comparable groups in other walks of life (Rook, 1954). Both these factors are at work in universities, and, since suicide is not a new phenomenon, it is surprising how little information is available about it as a cause of student deaths.

The period since the war has seen the development of student health services at almost every British university, and in this time much has been learnt about the physical and mental troubles of students. One of the most striking findings has been the comparatively high incidence of mental illness; though much of it has been of a trivial nature, it has sometimes interfered with study, sometimes wrecked a university career, and even, on occasion, has resulted in suicide. A student population must contain a number of unstable and insecure individuals, and in addition there seems no doubt that universities tend to attract such people. Whether the high incidence of mental illness is of recent origin, or whether this has always been so, it is impossible to say, for there is little information about student illness before the war to use as a standard of comparison.

For various reasons the importance of mental ill-health in undergraduate life is apt to be hidden at the older English universities. One of the reasons is undoubtedly the college system, which breaks the university into a number of self-contained, somewhat isolated communities. When cases of mental ill-health do occur in a college they are naturally regarded as matters not for discussion, perhaps even something of which to be ashamed, so that the facts are confined strictly within bounds. In other instances the patient himself tries to keep his troubles secret, lest his university career should be affected, and so seeks help in London or elsewhere away from the university town. In consequence, though there have been indications that this is the most serious cause of undergraduate ill-health in Cambridge, it has not been possible to obtain accurate figures showing the incidence of mental trouble in the University as a whole.

The first real light to be shed on the subject came in 1951 when Parnell, working at the Institute of Social Medicine at Oxford, obtained information from some of the Oxford colleges about prolonged illness and mortality occurring among their undergraduates. When the figures were analysed two significant facts emerged: the considerable amount of serious mental illness, and the high incidence of suicide among Oxford undergraduates, which he estimated to be eleven times that of a similar group in the general population. These facts came as a surprise to university authorities, and that many responsible people were startled and shocked was obvious from the wide interest taken and the correspondence evoked in the national press.

The chief source of concern related to the problem of suicide. The questions which were raised were varied and the answers given often contradictory: What was the reason for the high incidence? ; Were certain classes of undergraduates specially liable? ; and, What steps should be taken in prevention? Some people apparently doubted the validity of the figures; others, while accepting that the suicide rate was high, put forward differing suggestions on the cause. Frustration over work and the fear of examinations were the most common suppositions, but this was emphatically denied by others. Some suggested that love affairs or financial worries were of greater moment, while one correspondent regarded the materialistic attitudes of the modern undergraduate to be the basic cause. Again, members of certain faculties were said to be specially liable, as were those men coming from poorer homes, who were often supposed to have difficulties in adjusting themselves to university life.

From the welter of conflicting opinions it was obvious that at the time little was known about the incidence of mental disturbance or about suicide rates in British universities. Many people, it seemed, held strong opinions on the subject, although the foundations on which such opinions could be based were acknowledged to be insecure.

Adolescent Suicides

Observers who have studied the question of adolescent suicide have emphasized the complexity of the problem and the many factors in causation that must be taken into account, factors which may have a considerable influence on the rates of incidence (Bakwin, 1957).

Different races adopt differing attitudes towards suicide; in some countries it is regarded to some extent as a noble and dignified act, while in others it is regarded as selfish and defeatist. Sometimes religious beliefs have an important influence, or social and economic factors may play a part, so that the rates of incidence vary even in different districts of the same town. In nearly all countries of the world the rates for women are considerably lower than those for men.

British universities, with mixed populations of students from all over the United Kingdom from all strata of society, and with more than a sprinkling of Commonwealth and foreign members, are a particularly difficult group for which to obtain a reliable basis of comparison. The figures published by the Registrar-General, while undoubtedly the best available, are not entirely satisfactory for this purpose. The chief drawbacks are that the age grouping of 15 to 19 years and 20 to 24 years used by the Registrar-General cuts across the usual age grouping of the student, of whom some are in the first group, with a greater proportion in the second. As the rate of suicide goes up steeply during the years of adolescence it is probably best to use the 20 to 24 age group, although not a strictly valid comparison. Secondly, no account is taken of socio-economic groupings, which, in a university population, obviously differ considerably from that of the ordinary population of England and Wales.

The incidence of suicide in England and Wales, in the age groups 15 to 19 and 20 to 24 during the years 1948 to 1956 inclusive given in the Registrar-General's tables, has shown little fluctuation. The highest annual rate per 100,000 living during this period was 7.57 for males in the 20 to 24 age group, and the lowest 0.71 per 100,000 living for women in the 15 to 19 age group.

Student Suicides

The commonest cause of undergraduate deaths known to the University Health Service during the 10-year period, from October 1, 1948, until September 30, 1958, was accident, followed closely by suicide. During this period there were 14 undergraduate suicides at Cambridge, 11 of them involving white British undergraduates and 3 involving coloured undergraduates. In Parnell's (1951) report suicide was responsible for 27% of the Oxford undergraduate deaths, being exceeded only by accident. A similar occurrence was reported from Yale University (Parrish, 1957) for the years 1920–55, when suicide was the second most frequent reason for student deaths during the period, causing 12% of all deaths. These percentages may be compared to those obtained from the Registrar-General's Statistical Tables. For the male population of England and Wales in the age group 20 to 24 years, during the years 1948 to 1956 inclusive, the corresponding figure was 4.7%.

Table I gives the incidence of suicide in certain British and American universities, and for comparison the rate in the general population of England and Wales for the age groups 15 to 19 years and 20 to 24 years. The period of observation varies somewhat, but in each instance it is a post-war period. The smallness of the number of suicides in all the universities must be stressed, for with so few cases it is only too easy to draw erroneous conclusions from statistical tables.

Table I brings out the low rate of women suicides in the social group who become university students. In the student population studied of just on 40,000, of which about 20% were women, there were only two woman suicides. It is apparent that when making comparisons of suicide rates, if total rates are used, universities with a high proportion of women are at an advantage compared with those where the proportion of women is low. Hence it is best to confine comparison to male students only.

TABLE I.—*Incidence of Student Suicides*

Group		Approximate Population (Yearly Average)	No. of Suicides	Period of Observation In Years	Annual Rate per 100,000 Living
England and Wales. Age 15–19	Men	1,302,000	331	9	2·8
	Women	1,389,000	134		1·1
	Total	2,691,000	465		1·9
England and Wales. Age 20–24	Men	1,394,000	767	9	6·1
	Women	1,462,000	282		2·1
	Total	2,856,000	1,049		4·1
Cambridge University	Men	5,950	13	10	21·8
	White men	5,600	10		17·8
	Women	630	1		—
	Total	6,580	14		21·3
Oxford University (Skottowe, 1957)	Men	5,250	16	10	30·5
	Women	800	—		—
	Total	6,050	16		26·4
Seven British universities	Men	15,000	10	8·5	7·9
	Women	5,000	—		—
	Total	20,000	10		5·9
University College, London (Malleson, 1957)	Men	2,500	3	7	17·1
	Women	1,000	1		—
	Total	3,500	4		16·3
Yale University (Parrish, 1957)	Men	3,290	15	35	13·0

A striking finding at Cambridge has been the high incidence of suicide in coloured undergraduates. In the average year there are about 350 dark-skinned students in residence, and the suicide of three of these men in the 10-year period gives a very high rate of incidence—85.7 per annum per 100,000 living, a figure which, in view of the smallness of the numbers involved, must be regarded with suspicion. It may be that the Asiatic regards suicide as less of a disaster than his British counterpart. Unfortunately few figures of suicide rates are available for Asiatic countries (Table II). Japan, because of the well-known attitude of the Japanese to suicide, must be treated apart, but Ceylon returns a rate which is high compared with other Commonwealth countries though not so high as in some parts of Europe.

TABLE II.—*Mortality From Suicide in Selected Countries. Yearly Average Rates per* 100,000 *Population of Males of Age Groups* 15–19 *and* 20–24

Country	Years of Observation	Age Group 15–19	Age Group 20–24
Europe:			
Denmark	1952–4	8·3	25·4
France	1952–4	4·4	7·4
Norway	1952–4	2·0	7·2
Sweden	1951–3	6·0	15·5
U.K.:			
England and Wales	1952–4	2·9	6·0
Scotland	1952–4	1·9	3·4
N. Ireland	1952–4	1·3	3·3
America:			
Canada	1952–4	3·8	7·3
U.S.A. Whites	1951–3	4·2	9·7
U.S.A. Non-Whites	1951–3	1·7	7·8
Asia:			
Ceylon	1952–4	5·9	16·1
Japan	1952–4	26·1	60·0

Compiled from *Epidemiological and Vital Statistics Report*, vol. 9, No. 4, 1956. World Health Organization.

It is easy to think of a number of reasons why coloured students should be under nervous stress. Besides the difficulties of study common to all students they have to contend with difficulties of homesickness, of language, of food, of climate, of other ways of life, and sometimes with considerable loneliness. The argument that these circumstances are a cause of a high rate of suicide would be more convincing if it were shown to apply to other universities. Actually in the seven universities, with a coloured population at least one-third greater than that of Cambridge, there were no suicides among these students. There is some evidence, however, that coloured students are more liable to mental illness than are white students, and it would seem fairest to keep the comparison to white male students only.

If this is done it will be seen that for the period in question the seven British universities had a suicide rate which is slightly higher than that of England and Wales: the rate at Cambridge is nearly three times, and that at Oxford is nearly five times, the rate for England and Wales.

Analysis of Cambridge Undergraduate Suicides

Eleven of the undergraduates committing suicide came from the United Kingdom, two were from India, and one was a Siamese; there were 13 males and one female; one was aged 19 years, five were 20, six 21, and one 22; in one instance the age is unknown.

It is difficult to assess the social group to which an undergraduate belongs without knowing a good deal about the home background, for the patterns of income have changed so much since the war that classifications used previously may be quite wrong. A rough classification of social groups may be made from the schools which undergraduates have attended, dividing them into the more expensive and the less expensive schools. With this method it appears that roughly half the undergraduates go to the more expensive schools, probably coming from better-off homes, and half go to less expensive schools. B. W. Davy (1958, personal communication), using more accurate methods for the five colleges covered by his research, came to very similar conclusions. As six of the suicides occurred in undergraduates who went to the higher-income-group schools and five occurred among those who had been to the lower-income-group schools, there is little suggestion that social class was a factor.

National Service had been completed in three instances, had been deferred in five, and in two the men had been rejected. Three men were not liable.

There were two suicides in two colleges at intervals of over two years, while the remaining ten were in different colleges. Two of the suicides were reading Law, two Natural Sciences, and the remaining ten were in separate faculties. In the examinations prior to suicide, one had been placed in Class I, three had been placed in Class II, Division I, four in Class II, two in Class III, two had failed, and two had not taken an examination. These results could be described as average or possibly rather below average.

Three men were in their first year of residence, eight in their second year, and one in the third year; the woman was in her third year. One man, who owing to mental ill-health had missed the usual third-year examination, was in his fourth year. Two periods of time seem to be of importance—near examination time and at the beginning of the academic year: there were five deaths in May, two in June, four in October, and one each in January, March, and April.

The precipitating factors were said in five instances to be worry over work. In two instances the men had been noted as restless and depressed, one man had a recurrence of symptoms of pulmonary tuberculosis which caused his mental upset, one man was in difficulty because of homosexuality, and in the case of the woman it was a love affair; in four instances apparently no one had noted that anything was amiss. Three of the cases were under psychiatric care at the time of the suicide, one had been seen a short time previously by a psychiatrist but had refused to attend again, and one was under the care of a general practitioner. In four cases there were indications of home difficulties. The cause of death in nine cases was carbon monoxide poisoning, two men shot themselves, two hanged themselves, and one died from drugs. Six deaths occurred in college rooms, one in a college hostel, three in lodgings, one in hospital, one in some woods just outside the town, one at home during vacation, and one in a foreign country.

The preponderance of carbon monoxide poisoning as a means of committing suicide suggests that methods of heating other than gas are to be preferred in colleges and hostels. It must, however, be noted that only two out of ten suicides in the seven universities made use of gas. If an individual is determined to kill himself there are always a number of methods available.

Undergraduate Suicides in Former Years

Through the kindness of Dr. C. G. Eastwood, medical officer of health for the City of Cambridge, it has been possible to obtain information about undergraduate deaths occurring during term in the 20 years prior to the setting up of the University Health Service. There are gaps of three years in the records, which have been filled to some extent from other sources, and the register is not as complete as for the last 10 years, when watch has been kept for undergraduate deaths not only in term time, but during vacation. In Table III is given the incidence of male undergraduate suicides for three 10-year periods; these rates represent a minimum, especially in the earlier years, when cases may easily have been missed, especially if death had occurred elsewhere than at Cambridge.

TABLE III.—*Incidence of Male Undergraduate Suicides at Cambridge University Since October*, 1928, *Given in Decades*

Years	Estimated Male Undergraduate Population	No. of Suicides	Annual Rate per 100,000 Living
October, 1928, to September, 1938	4,814	10	Total 20·8
October, 1938, to September, 1948	3,693	12	,, 32·5
October, 1948, to September, 1958	5,950	13	,, 21·8 White-skinned 17·8

The incidence of suicide of white undergraduates was highest in the decade which included the war. The war years brought many changes to the University, some of which may have influenced the suicide rate; the undergraduate population decreased, the more physically efficient and to some extent the more mentally stable men were absorbed by the armed Forces, so that the type of entrant differed from that of peacetime. In addition there were the trials of bombing and the anxieties which are inseparable from international strife.

The previous decade, from the late 'twenties until a year before the outbreak of war, is more comparable to the last 10 years, but there are still important differences. Since the war there has been an increase in the number of undergraduates, and in the earlier post-war years a high proportion was made up of men who had returned from war service. Whether these, or other differences, have had an influence on the suicide rate it is impossible to say, but actually the rates during these two decades are very similar. During a period of 35 years 103 undergraduate deaths, excluding war deaths, are known to have occurred, most of them in term time; of these, 41 were due to accident, 27 to disease, and 35 to suicide.

Discussion

The considerable differences in the rates of suicide found in the older English universities compared with those found in most other universities, and in the country as a whole, are not easily explained. The foregoing analysis of suicides occurring at Cambridge in the last 10 years has shown a rather remarkable spread in the various socio-economic factors which affect the undergraduates' existence. It is apparent that no one factor is involved, but that a number of factors, while not directly causal, may aggravate an underlying tendency to mental disturbance.

In trying to come to some conclusions two possibilities must be considered. Firstly, have the older universities some special attraction for the mentally unstable, or is it possible that the selection methods adopted in some way favour such a choice? Secondly, what are the differences in the mode of life or methods of study at the older universities which could act as aggravating factors tending to unbalance someone with an already unstable personality?

It must be acknowledged at once that no satisfactory answer can be given to the first question. It is probable that the children of highly intellectual, and of highly ambitious, parents form a higher percentage of entrants at Oxford and Cambridge than they do elsewhere. These parents often expect much of their children or, what comes to the same thing so far as mental stress is concerned, the children believe they do and so ask much of themselves. Pressure to do well in competitive examination, whether real or fancied, can be a potent cause of anxiety and worry. If the more obsessional students would accept Jowett's advice, that the class does not matter, fewer would suffer from psychoneurotic symptoms.

Selection methods for university entrance are under such close and constant scrutiny that it seems unlikely that the methods differ greatly in the various British universities; where Oxford and Cambridge do differ is that competition for places is more acute than elsewhere. It has been suggested that this leads to higher standards being used and that the "hazard of suicide marches hand in hand with the severity of selection," the implication apparently being that higher standards of entry are more likely to lead to the selection of the mentally unstable. This idea has not, however, found universal acceptance. It does seem possible that the difficulties of entry, when they are surmounted, lead in some cases to exaggerated hopes which are doomed to disappointment, and they may even produce in some individuals a faith in his or her abilities which must sooner or later be dispelled, possibly with unpleasant effect. In order to answer this first question with any degree of certainty it would be necessary to have a great deal more basic knowledge together with accurate figures about the amount and type of mental ill-health occurring in the University. For reasons which have already been indicated no such figures are available from which to construct a reliable estimate.

A number of points can be made bearing on the second question.

The transition from schoolboy to student is not without difficulties for which some individuals are ill prepared. This is particularly likely to occur when the change is from those schools which favour the more intensive forms of training to one of the older universities where the undergraduate is left much to his own devices as regards planning the reading for his examination. Added to this is the need for concentrating the work and the many other activities that are crowded into the undergraduate's daily life into an eight-weeks term. In other universities it is probable that a small degree of compulsion makes transition not quite so abrupt; it may even increase the sense of security and the feeling of being one of a herd. The intellectual freedom so much a feature of the older university may foster self-reliance in a majority of undergraduates, but in the weaker members it may lead to a sense of loss of direction and a feeling of inadequacy.

A fundamental distinction between life at Oxford and Cambridge and other universities, and one which may have an influence on the suicide rate, is the great difference in the number of residential students and those living in their own homes while attending their course. While there is much to be said for the college system, with its encouragement of extracurricular activities, it seems probable that living at home has a stabilizing influence even though the waking hours spent there are few. The college staircase may facilitate study, but it can also lead to loneliness and can encourage brooding.

Money worries are often suggested as a cause of psychological trouble in undergraduates, and though there must be a considerable disparity between financial means of individuals, most observers believe that financial troubles only rarely induce nervous symptoms.

It is difficult to estimate the part played by fear of examinations, to which must be added fear of loss of grant unless certain standards are reached, but in some instances this is undoubtedly a cause of serious anxiety. Despite dogmatic statements to the contrary, it is difficult to believe that examinations did not have some influence on the Cambridge suicides, for over half of them occurred around the examination period, and four out of five of those who were believed to be worrying over their work died in May. It should, however, be realized that, in the Registrar-General's returns, and in the returns from some other countries, the months of April, May, and June show an increased incidence when compared with other months. It must also be pointed out that the apparent increase of liability near examination time is not shown in the two previous decades. In any case neither financial nor examination worries are confined to Oxford and Cambridge, though it is possible that both may be sources of stress which are more acute there than they are elsewhere. It has, for instance, been suggested that the examinations at redbrick universities follow more closely to the lectures that are given and in consequence are less likely to be a cause of undue strain.

Although there is no evidence at Cambridge that undergraduate suicides have increased in number in recent years, certain post-war developments may have had an adverse effect. One of these has been the increase in the number of students, which adds to the difficulties of supervision even though the tutorial body may have been strengthened to some extent; in the period 1948 to 1957 the numbers at Cambridge have increased by over 1,200. In a big university the detection of the earliest stages of mental ill-health must almost inevitably fall on those with whom undergraduates are in daily contact. When it is suspected that trouble is brewing the patient can be guided to where specialized help can be obtained. The increase in the number of undergraduates must mean that tutors find it more difficult to get to know each man personally so that they are in a position to detect small, but possibly significant, changes in personality or performance. Nor do present economic trends make this part of a tutor's work any easier. That cases of mental ill-health are sometimes not detected in the earliest stages is unfortunate, but under present conditions is not surprising.

The crux of the problem has recently been admirably summed up by one of Her Majesty's coroners: "The truth is that suicide is a most complex phenomenon and highly unpredictable; our knowledge of its roots is scanty indeed" (Thurston, 1958). Student suicides are an end stage of the problem of mental health in universities about which undoubtedly far too little is known even by those most directly concerned. Figures of incidence of mental ill-health have been given for certain universities (Still, 1954; Malleson, 1954), but none are available for those universities with the highest incidence of suicide. Information and statistics are the bricks and mortar of prevention, and until mental disease in university students is regarded in the same way as any other illness, as a misfortune and not something of a stigma, it is unlikely that much progress will be made in preventing its occurrence.

Summary

The incidence of undergraduate suicides at the older English universities during a 10-year post-war period is higher than it is in other comparable groups.

The factors which may have had an influence on the rate are discussed.

The need is stressed for more information about the incidence and the various ecological factors which affect the mental health of undergraduates.

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SECRETION OF BLOOD GROUP ANTIGENS AND PEPTIC ULCER

BY

C. A. CLARKE, M.D., F.R.C.P.

D. A. PRICE EVANS, M.B., M.Sc., M.R.C.P.

R. B. McCONNELL, M.D., M.R.C.P.

AND

P. M. SHEPPARD, M.A., D.Phil.

From the Departments of Medicine and Zoology, University of Liverpool

We have shown that in the Liverpool area there is a higher frequency of blood group O in patients with duodenal ulcer than in a control group taken from the general population (Clarke *et al.*, 1955). In gastric ulcer, on the other hand, we found no evidence for an association with group O, despite the fact that Aird *et al.* (1954) and several subsequent writers, discovered it in other populations. Later we showed that there was a higher frequency of non-secretors of ABH substances among duodenal ulcer patients in Liverpool than in a control series from the general population (Clarke *et al.*, 1956). In a family study of duodenal ulcer sibships, however, where the unaffected sibs acted as controls, we found no evidence that group O individuals were significantly more likely to have an ulcer than their A, B, or AB sibs. The evidence regarding the association between non-secretion and duodenal ulcer within families was equivocal, but with the collection of further sibships the association has now almost disappeared (Clarke, 1959).

The present paper is concerned with the following aspects of the subject: (1) the ABH secretor frequencies in gastric and duodenal ulcer in Liverpool; (2) an examination of the apparent liability to duodenal ulcer of individuals with different ABO blood groups and secretor status; and (3) a review of some of the hypotheses on the nature of the association between ABH non-secretion and duodenal ulcer and the presentation of fresh evidence on the subject.

Secretor Character in Duodenal and Gastric Ulcer

Table I gives the results of our investigations, started in 1954, and Table II the statistical analysis. It will be seen that whilst there is a striking association between duodenal ulcer and ABH non-secretion, there is no evidence that in Liverpool there is any association between gastric ulcer and ABH non-secretion; moreover, there is a significant difference between duodenal and gastric ulceration with respect to the frequencies of ABH non-secretion (36.6% in duodenal and 27.5% in gastric ulcer; controls 24.3%).

The degree of association between both duodenal and gastric ulcer and group O varies from place to place (Roberts, 1957). In Liverpool, where an association of group O with duodenal ulcer but not with gastric ulcer was found, non-secretion is similarly associated with duodenal ulcer and not with gastric ulcer. It is therefore important to establish whether in other localities the degree of association between the two diseases and group O is correlated with that between the diseases and non-secretion. If a correlation be found it would suggest that both group O and non-secretion were working in the same way and that their mode of action is possibly immunological. If no

TABLE I.—*Secretor Status of Series of Controls* (851), *Duodenal Ulcers* (1,014), *and Gastric Ulcers* (138), *Not Random for Blood Group*

Phenotype	Control		Duodenal Ulcer		Gastric Ulcer	
	Males	Females	Males	Females	Males	Females
O secretor ..	131	135	284	60	28	18
O non-secretor ..	35	43	168	40	9	9
A secretor ..	165	117	194	35	28	15
A non-secretor ..	58	44	94	23	8	7
B secretor ..	47	29	37	13	4	6
B non-secretor ..	16	7	30	5	2	3
AB secretor ..	11	9	17	3	1	—
AB non-secretor	—	4	10	1	—	—

TABLE II.—*Statistical Analysis of Data in Table* I

Comparison of frequency of non-secretors between:

	d.f.	χ^2	Probability
1. The various ABO blood group classes in:			
Control males	2 ..	1·43 ..	>0·3
,, females	2 ..	0·68 ..	>0·7
Duodenal ulcer males ..	2 ..	3·41 ..	>0·1
,, ,, females ..	2 ..	1·30 ..	>0·5
Gastric ulcer males ..	1 ..	0·01 ..	>0·9
,, ,, females ..	1 ..	0·01 ..	>0·9

(In the first four of the above comparisons, because of the small numbers, AB has been combined with B; in the fifth and sixth comparisons AB and B have been combined with A.)

2. Males and females:			
Control	1 ..	0·34 ..	>0·5
Duodenal ulcer	1 ..	0·29 ..	>0·5
Gastric ,, ...	1 ..	1·37 ..	>0·2
3. Control and duodenal ulcer	1 ..	32·54 ..	≤0·001
4. ,, ,, gastric ,,	1 ..	0·66 ..	>0·3
5. Duodenal ,, ,, ,,	1 ..	3·96 ..	<0·05

correlation be found it would suggest either that the two factors work in different ways (probably neither immunological) or that stratification of the population is responsible for at least one of the associations. Stratification seems very unlikely (see Roberts, 1957), but it has not formally been disproved.

Liability to Duodenal Ulcer of Different Blood Group and Secretor Phenotypes

Previous assessments of the risk to individuals of the different blood group and secretor phenotypes of developing duodenal ulcer (*Brit. med. J.*, 1958) have been arrived at by calculations based on series giving blood group frequencies and a separate series, such as that in Table I, giving secretor status, but not random for blood group (Clarke *et al.*, 1956; Wallace *et al.*, 1958). No one, so far as we know, has published a random series of ulcer patients and controls. The data in Table III are from 521 consecutive duodenal ulcer patients collected between January 1, 1956, and March 31, 1958, and are independent of the series of duodenal ulcer patients reported by Clarke *et al.* (1955), but not independent of those in Table I.

TABLE III.—*Phenotypes in Series of Duodenal Ulcer Patients and Controls, Random for Blood Group and Secretor Status*

Phenotype	Control Series		Duodenal Ulcers		Per Cent Incr. or Decr. on Control
	No.	%	No.	%	
O secretor	245	36·03	186	35·70	− 0·9
A ,, ...	204	30·00	124	23·80	−20·7
O non-secretor ..	70	10·30	98	18·81	+82·6
A ,, ..	75	11·03	62	11·91	+ 7·9
B secretor	54	7·94	19	3·63	−54·3
B non-secretor ..	15	2·21	19	3·63	+64·25
AB secretor	14	2·06	10	1·94	− 5·88
AB non-secretor ..	3	0·44	3	0·58	+31·82
Total ..	680	100·01	521	100·00	

TABLE IV.—*Apparent Liability to Duodenal Ulcer of Different Phenotypes*

Phenotype	Expected Duodenal Ulcer	Controls	"Risk"
O non-secretor	174	70	2·49 : 1
A, B, and AB non-secretor ..	149	93	1·60 : 1
O secretor	331	245	1·35 : 1
A, B, and AB secretor	272	272	1·00 : 1

The 680 controls are a random series of doctors, technicians, students, nurses, and Liverpool Territorial Army soldiers collected between September 1, 1955, and March 31, 1958. The same techniques were employed in scoring both patients and controls, an extract of the seeds of *Ulex europaeus* being used throughout as an anti-H. It can be seen that the four categories of ABH non-secretor all show an increased incidence in the disease group, whilst the four ABH secretor phenotypes would each appear to have some degree of protection, thus indicating that the secretor locus is having a bigger effect on duodenal ulcer than the ABO locus.

In order to calculate the liability to ulcer of the different phenotypes, Dr. Richard Doll has suggested that one should take as a baseline the least susceptible group. He has compiled for us Table IV, in which the numbers of groups B and AB, being too small for any great reliance to be placed on them, have been combined with group A. The figures for "expected duodenal ulcer" in each phenotype in this table were obtained by multiplying the number of duodenal ulcers in Table III by 272/153, so as to make equal the numbers of duodenal ulcers and controls in the A, B, and AB secretor phenotype. It can be seen that group O non-secretors would appear to be 2.49 times more liable, and the A, B, and AB non-secretors 1.60 times more liable to develop duodenal ulcer than are A, B, and AB secretors. Taken at their face value, the data suggest that the liability to ulceration due to being simultaneously O and non-secretor is more than would be expected from the additive effects of the two phenotypes, and indicate that they interact with one another. However, the analysis reveals that the excess liability is not statistically significant.

It must be emphasized, however, that these assessments have been made using the general population as a control. When this type of analysis is applied within families the results are very different. Table V shows the numbers of the eight phenotypes in a series of duodenal ulcer patients, random for blood group and secretor status, who also have an unaffected sib whom we have studied. The phenotypes of the sibs are also shown—one for each of the patients, and where more than one unaffected sib has been tested the oldest has been used as the control. The phenotypes are in the order of susceptibility deduced from Table III, and one would expect to have relatively more ulcers in the top half of the table and more controls in the bottom half. Even remembering the expected correlation between the phenotypes of sibs, the almost exact equality of the numbers of the different phenotypes is remarkable. Both the patients and their unaffected sibs have much higher

TABLE V.—*Numbers of Duodenal Ulcer Propositi and Oldest Unaffected Sibs Examined, Subdivided into Phenotypes*

Phenotypes	Either Sex		Same Sex	
	Ulcer	Sib	Ulcer	Sib
O non-secretor	42	37	20	20
B ,, ...	5	7	4	4
AB ,, ...	4	3	2	1
A ,, ...	28	28	13	13
O secretor	90	91	47	46
AB ,, ...	6	5	5	3
A ,, ...	59	61	26	31
B ,, ...	15	17	10	9
Total ..	249	249	127	127

group O and non-secretor frequencies than the general population, and this must mean that their mothers and/or their fathers had high O and high non-secretor frequencies. Since non-secretor frequencies are probably very uniform throughout Europe this is very unlikely to be due to their being from a particular racial strain, and therefore it is unlikely to be coincidental that one or more of their offspring have developed duodenal ulcer.

While we think that the sibship results are remarkable, yet the data are not extensive enough to prove a discrepancy between them and the results using the general population as a control. Because of this, and in view of the almost universal finding of the association with group O and the finding with non-secretor in Scotland (Wallace *et al.*, 1958), we propose to consider possible biochemical or serological explanations for the associations.

Nature of the Association Between ABH Non-secretion and Duodenal Ulcer

Several hypotheses have been put forward which might explain the relationship between duodenal ulceration, group O, and ABH non-secretion. Thus Aird (1955) thought that the various blood group substances might confer different degrees of protection against ulcerogenic agents, while Clarke *et al.* (1956) suggested that there might be a differential protection depending on the interrelationship between ABH and Lewis blood group secretion. The hypothesis that the excess of group O in duodenal ulcers is due entirely to H substance protecting less than A or B substances is refuted by the present data (Table IV), since, in the absence of H secretion (that is, in non-secretors), there should be no difference in the liability of O and non-O people. In fact, in our data there is a significant excess of group O amongst the duodenal ulcer non-secretors ($\chi^2=4.1$; $P<0.05$) compared with the control non-secretors. In neither hypothesis was it indicated whether the basis of the protection was immunological or mechanical—that is, coating of the duodenal mucosa by the mucoid blood group substances. Cain (1957) put forward a suggestion which would depend on an immunological mode of action.

We can now present the results of two investigations which throw some light on the question of a purely mechanical explanation of the susceptibility of ABH non-secretors.

Amounts of Blood Group Substances in the Saliva of Secretors and Non-secretors of ABH

Professor W. T. J. Morgan has pointed out to us that since non-secretors of ABH usually secrete much more Le^a than do ABH secretors, there may not be a great difference in the amount of blood group substance in the gastro-intestinal tract of secretors and non-secretors. In an attempt to test whether or not this is so, one of us (D. A. P. E.) has investigated the fucose content of saliva from 213 ABH secretors and 119 non-secretors of different ABH blood groups (fucose is a rare sugar found in large amounts in blood group substances; only very small amounts have been found elsewhere in the human body). A modification of Gibbons's (1955) method for methyl pentose was used. All subjects were free of duodenal and gastric ulcer symptoms.

It will be seen from Tables VI and VII that the ABH non-secretors produce a lower mean salivary concentration of fucose than the ABH secretors, and that the B secretors have a higher mean concentration than the O secretors. There are significant correlations between fucose content and serological activity, with the exception of A activity in A secretors (Table VIII).

TABLE VI.—*Mean Log_{10} Salivary Fucose Concentrations for Non-ulcer Salivas*

Phenotype	No.	Mean Log_{10} Salivary Fucose	Standard Error of Mean	Antilog of Mean (μg./ml. Fucose)
O secretor	94	1·9009	0·01812	79·60
A ,,	62	1·9257	0·021137	84·28
B ,,	57	1·9758	0·026756	94·58
O non-secretor	57	1·8187	0·026800	65·88
A ,,	53	1·8091	0·02522	64·43
B ,,	9	1·7561	0·03806	57·03

TABLE VII.—*Comparison of Means of Log_{10} Salivary Fucose Values by Means of "t" Test*

Phenotypes Compared	Value of "t"	Degrees of Freedom	Significance of "t"
O secretor –B secretor	2·399	149	$p<0.02$
A ,, –B ,,	1·481	117	$p>0.10$
O ,, –O non-secretor	2·631	149	$p<0.01$
O ,, –A non-secretor	2·995	145	$p<0.01$
O ,, –B ,,	2·418	101	$p<0.02$
A non-secretor–B ,,	0·651	60	$p>0.10$
O ,, –B ,,	0·902	64	$p>0.10$

TABLE VIII.—*Correlation Between Log_{10} Salivary Fucose Content and Haemagglutination-Inhibition Titre*

Phenotype	Serological Activity Examined	Type of Antibody	No. of Salivas Examined	Correlation Coefficient r	Significance of r
Controls:					
O secretor	H	*Ulex*	94	0·5479	$p<0.001$
A ,,	A	Human	62	0·1482	$p>0.10$
A ,,	H	*Ulex*	62	0·5202	$p<0.001$
B ,,	B	Human	57	0·2785	$p<0.05$
B ,,	H	*Ulex*	57	0·3315	$p<0.02$
O non-secretor	Le^a	Human	52	0·3275	$p<0.02$
Duodenal ulcer:					
O secretor	H	*Ulex*	82	0·5374	$p<0.001$
O ,,	H	Eel	88	0·4957	$p<0.001$

TABLE IX.—*Calculation of Total Salivary Blood Group Content*

Phenotype	Mean Salivary Fucose μg./ml. (Note A)	Subdivision of Mean Salivary Fucose Content. μg./ml. (Note B)	Fucose Content of Pure Blood Group Substances (Note C)	Blood Group Substance Content. μg./ml. (Note D)	Total Salivary Blood Group Substance Content. μg./ml.
O, A, and B non-secretor	64·5	All Le^a	12%	537·5	537·5
O secretor	79·6	Lewis: 37·1	12%	309·2	521·7
		H : 42·5	20%	212·5	
A ,,	84·3	Lewis: 37·1	12%	309·2	562·6
		H : 15·9	20%	79·5	
		A : 31·3	18%	173·9	
B ,,	94·6	Lewis: 12·4	12%	103·3	557·5
		H : 4·5	20%	22·5	
		B : 77·7	18%	431·7	

A. Mean salivary fucose contents are from Table VI.

B. The mean salivary fucose concentrations have been ascribed to the various blood group substances as follows: (1) Non-secretors of ABH are presumed to secrete Lewis substance only. This is assumed to be Le^a. (2) H activity and log_{10} fucose concentration are correlated in O secretors. The intercept of the regression line is taken to represent fucose due to the Lewis substance present. This (when antilogged) is 37·1 μg./ml. The fucose content of this Lewis substance is taken to be that of Le^a—that is, 12%. (3) Since fucose correlates with H activity in all ABH secretors the ratios of fucose due to H substance in the various ABH secretors are taken to be the same as the ratios of the mean anti-H (*Ulex*) inhibiting power—namely, B sec.: A sec.: O sec.:: 1·68: 5·97: 16·00 μg./ml. Therefore the fucose due to H in A secretors is $42·5 \times 5·97 \div 16·00 = 15·9$ μg./ml., and the fucose due to H in B secretors is $42·5 \times 1·68 \div 16·00 = 4·5$ μg./ml. (4) Grubb (1951) showed that the approximate ratio of Le^a activity in ABH secretors was: groups A and O: groups B and AB:: 3: 1. It is assumed that A secretors and O secretors have equal amounts of Lewis substance in their salivas. Since 37·1 μg. of fucose per ml. was held to be due to Lewis in O secretors, the same amount is held to be present in A secretors. In B secretors the Lewis substance is held to account for $37·1 \div 3 = 12·4$ μg. of fucose per ml. This Lewis substance is assumed to have the same fucose content as Le^a. (5) The questions of (*a*) Lewis non-secretor persons and (*b*) Le^a secretion have been ignored in compiling this table.

C. The percentages of fucose are those in pure blood group substances obtained from ovarian cyst fluids (W. T. J. Morgan, 1958, personal communication).

D. Figures of blood-group-substance content are calculated by multiplying the figure of the mean salivary fucose content by the reciprocal of the fraction of fucose in the pure substance—for example, for non-secretors $64·5 \times 100 \div 12 = 537·5$ μg./ml.

The total salivary concentration of blood group substance has been computed for the different phenotypes, and the results are given in Table IX. The reasons for ascribing proportions of the mean salivary fucose concentration to the various blood group substances are given as footnotes to Table IX.

It will be seen that, as judged by the mean $\log_{10}$ salivary fucose content, the total amount of blood group substance is of the same order in each of the blood group and secretor subdivisions. It is true that the estimated proportions of different blood group substances present in each type of individual used in our calculation are only an approximation, but a radical change in the proportions ascribed is required materially to influence the figures computed for total blood group substance. So great a change would seem to be inconsistent with independent serological findings (see Race and Sanger, 1958).

The results of the biochemical investigations (see Tables VIII and IX) show that the fucose content is a good index of the total amount of blood group substances if the ABO blood group and secretor status is known. Fucose estimations indicate that there is little difference in the amount of blood group substances in the saliva of secretors and non-secretors. A full account of this work will be published elsewhere.

Comparison of Duodenal Ulcer Patients and Controls for Titre of Blood Group Substances and for Fucose Content of Saliva

If the ABH secretion itself protects mechanically against ulcer, secretors who develop an ulcer may tend to produce less blood group substances in their watery secretions than secretors who do not develop one. To test this hypothesis we investigated a secretor propositus and one of his unaffected secretor sibs who had the same blood group, to see if the titre of antigen was different in the two individuals. In 98 sib pairs studied the propositus secreted less antigen in 27 pairs, more in 29 pairs, and the same amount in the remaining 42 pairs. Thus these data again do not support the hypothesis of mechanical protection by the mucoid ABH substances, but are consistent with an all-or-nothing effect.

It will be seen from Table X that we have also compared the titres of the group-specific substances in the patients' saliva with the titres in the sibs and in some population controls. There is no evidence of a difference between the patients and their unaffected sibs. There is, however, a highly significant difference between the patients and their sibs on the one hand and the general population on the other, the mean titre of the general population sample being less with each of the antigens. Although the same standard salivas were used as technique controls throughout, it may be that this difference is not real but due to technical factors, as the controls were titred at a different time from the patients and their sibs. Therefore little reliance need be attached to this finding until the matter has been reinvestigated, but if later work shows that the secretor ulcer patients indeed secrete more than the general population secretors, this also would militate against the hypothesis of mechanical protection. There is apparently less variability in the controls than in the duodenal ulcer patients and their sibs (see also the findings with fucose below).

The salivary fucose contents of O secretors and O non-secretors with duodenal ulcer have been determined (Table XI); they have log normal distributions. Comparison of means (Table XII) shows that: (*a*) the O secretors, with and without duodenal ulcer, have means which are not significantly different; (*b*) similarly, the O non-secretors with and without ulcer have means which are not significantly different; and (*c*) both series of O non-secretors are significantly lower than both series of O secretors.

TABLE XI.—*Mean $\log_{10}$ Salivary Fucose Contents of Duodenal Ulcer Patients*

Phenotype	No. Examined	Mean $\log_{10}$ Fucose Value	Standard Error of Mean	Antilog of Mean (μg. ml. Fucose)
O secretor	89	1·9339	0·022643	85·88
O non-secretor ..	50	1·7545	0 036055	56·82

TABLE XII.—*Comparisons of Mean $\log_{10}$ Salivary Fucose of Duodenal Ulcer and Non-ulcer Subjects by Means of "t" Test*

Phenotypes Compared	Value of "t"	Degrees of Freedom	Significance of "t"
D.U. O sec.: D.U. O non-sec.	4·427	137	$p<0·0001$
,, : non-D.U. O sec.	1·144	181	$p>0·10$
,, : ,, non-sec. ..	3·245	144	$p<0·01$
D.U. O non-sec.: non-D.U. O sec. ..	4·051	142	$p<0·001$
,, ,, : non-D.U.O. non-sec. ..	1·451	105	$p>0·10$

The variances of the $\log_{10}$ salivary fucose concentrations are significantly higher in the duodenal ulcer subjects than in the non-ulcer subjects, both in secretors ($p<0.01$) and in non-secretors ($p<0.01$), and these results indicate that there is a real difference in variance of blood group substances in saliva between duodenal ulcer subjects and controls. This difference may be due simply to a greater variability of saliva flow induced by the disease, or by the circumstances at the time of collection of the samples.

The $\log_{10}$ salivary fucose content in the duodenal ulcer O secretors correlates with the titre of H substance using two different antibodies, eel serum and *Ulex* extract (Table VIII). The points where the two regression lines intercept the ordinate are not significantly different from each other nor from that of the non-duodenal ulcer O secretors.

Thus the serological data suggest that within any one blood group there is no difference between the amount of A, B, or H substances secreted by secretors with duodenal ulcer and their sibs. The

TABLE X.—*Results of Agglutination-inhibition Tests of Saliva of Duodenal Ulcer, Sib, and General Population Secretors*

Blood Group	Antisera or Lectin		Total No.	Titre of Saliva, 1 in										
				2	4	8	16	32	64	128	256	512	1,024	2,048
O	*Ulex*	D.U.	54	—	—	—	—	6	10	15	9	11	2	1
		Sibs	54	—	—	—	—	5	11	10	15	9	3	1
		Controls	92	—	—	2	3	17	27	36	6	1	—	—
A	Anti-A	D.U.	35	—	—	—	1	4	12	9	5	3	1	—
		Sibs	35	—	—	—	—	3	10	7	8	5	2	—
		Controls	58	—	—	1	1	16	20	15	4	1	—	—
A	*Ulex*	D.U.	35	—	—	1	8	13	9	—	4	—	—	—
		Sibs	35	—	—	1	6	13	8	3	3	1	—	—
		Controls	58	—	—	5	28	19	6	—	—	—	—	—
B	Anti-B	D.U.	10	—	—	—	—	—	2	—	1	3	2	2
		Sibs	10	—	—	—	—	—	1	—	2	3	3	1
		Controls	57	—	—	—	—	1	6	12	16	19	3	—
B	*Ulex*	D.U.	10	—	1	3	2	1	3	—	—	—	—	—
		Sibs	10	—	2	2	2	2	1	—	1	—	—	—
		Controls	57	1	18	36	2	—	—	—	—	—	—	—

biochemical evidence goes even further in suggesting that there is no difference in the total amounts of blood group substance between all duodenal ulcer patients and controls. It would seem, therefore, that if the association between group O, non-secretion, and duodenal ulcer is causal (but not due to a pleotropic effect of the genes) the most probable explanation can be found in the differences between the antigenic properties of the A, B, H, and Lewis group-specific substances, and this would imply that there is an immunological factor in the pathogenesis of duodenal ulcer (see Clarke *et al.*, 1957).

Conclusions

Gastric and duodenal ulcer in Liverpool behave differently with respect to the frequency of secretion and non-secretion of ABH blood group substances, there being no apparent association between non-secretion and gastric ulcer.

The excess of group O individuals in a duodenal ulcer series compared with a general population control is as great in the secretor as in the non-secretor patients. Group O non-secretors are more than twice as liable to develop duodenal ulcer as secretors of groups A, B, and AB.

Evidence is presented that the fucose content of a saliva specimen is a good index of its content of total blood group substances, provided the ABO blood group and ABH secretor status is known. Fucose estimations in saliva specimens indicate that the various types of ABH secretors and non-secretors all secrete about the same total amount of blood group substances.

There is little difference between the mean salivary titre of A, B, and H substances of secretors with duodenal ulcer and their unaffected sibs. The mean salivary fucose concentration, and hence the total blood group substance concentration, are the same in duodenal ulcer patients as in controls. These results suggest that the protection enjoyed by ABH secretors is not due to the blood group substances protecting quantitatively. The most probable explanation of the associations found between group O, non-secretion, and duodenal ulcer is that there is an immunological factor in the pathogenesis of duodenal ulcer.

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EXCESS BLOOD-GROUP SUBSTANCE A IN SERUM OF PATIENT DYING WITH CARCINOMA OF STOMACH

BY

M. BARBER, B.Sc.

AND

I. DUNSFORD, Ph.D.

National Blood Transfusion Service, Sheffield

The following observations are reported because they may throw some light on the association between blood group A and carcinoma of the stomach (Aird, Bentall, and Roberts, 1953).

Case Report

Mrs. J. was admitted to the Sheffield Royal Infirmary after a severe haematemesis, and it was necessary to select blood because of her anaemic and shocked condition. The duty pathologist grouped Mrs. J., by both tile and tube techniques (Dunsford and Bowley, 1955), and obtained the following results: anti-A, − ; anti-B, − ; O serum, (+) ; A cells, − ; B cells, V ; O cells, − ; auto-control, −. These results suggested that Mrs. J. was a rare subgroup of A—possibly A_4 (Dunsford and Aspinall, 1952)—and the sample was immediately referred to one of us (I. D.) for opinion. On regrouping the same sample of blood, the following results were obtained: anti-A, V ; anti-B, − ; O serum, V ; A cells, − ; B cells, V ; O cells, − ; auto-control, −. It will be observed that Mrs. J.'s blood now gave the reactions expected of a group A blood. Following a telephone discussion with the pathologist carrying out the original grouping, the only difference in method and reagents used lay in the fact that the cell grouping done at the Sheffield Royal Infirmary was on unwashed red cells, whilst the grouping at the Blood Transfusion Service Laboratories was on washed cells—that is, cells freed from the patient's serum by centrifuging through three aliquots of isotonic saline. This suggested that Mrs. J.'s serum contained enough A substances to neutralize the anti-A antibodies before they could agglutinate her red cells.

This possibility was investigated, and to one volume of Mrs. J.'s washed red cells (4% in saline) was added one volume of her serum, and this mixture was then tested with standard anti-A, anti-B, and group O sera. As a control Mrs. J.'s 4% washed red cells were mixed with an equal volume of saline, and this mixture was tested with the same antisera. The results obtained are shown in Table I. It will be seen that the addition of Mrs. J.'s serum to her red cells inhibits the action of anti-A grouping serum and greatly reduces the action of group O sera.

TABLE I

	Anti-A (Batch No. 973)	Group O (Batch No. 92)
Mrs. J.'s cells in saline plus Mrs. J.'s serum	—	w
Controls " " " " saline	V	V
	V (A_2)	V
	— (O)	—

TABLE II.—*Serial Dilutions of Sera from Mrs. J. and Five Normal Group A Subjects to which Anti-A 963 Diluted 1/8 was Added*

Subject	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Mrs. J. ..	–	–	–	–	–	w	gw	+	+	+	+	++	++
x/80919 ..	+	+	+	+	+	++	++	++	++	++	++	++	++
x/80922 ..	+	+	+	+	+	++	++	++	++	++	++	++	++
x/80918 ..	+	+	+	+	+	++	++	++	++	++	++	++	++
x/80921 ..	+	+	+	++	++	++	++	++	++	++	++	++	++
x/80223 ..	(+)	(+)	+	++	++	++	++	++	++	++	++	++	++

TABLE III.—*Serial Dilutions of Sera from Mrs. J. and Four Blood Donors to which Anti-A 805 Diluted 1/8 was Added*

Subject	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Mrs. J. ..	–	–	–	–	–	?	gw	(+)	(+)	(+)	(+)	(+)	+
x/82372 ..	?	w	w	gw	gw	+	+	++	++	++	++	++	++
x/82385 ..	(+)	(+)	(+)	(+)	+	++	++	++	++	++	++	++	++
x/82388 ..	(+)	(+)	(+)	(+)	+	+	++	++	++	++	++	++	++
x/82390 ..	gw	(+)	(+)	(+)	+	+	++	++	++	++	++	++	++

The next part of the investigation was to determine the amount of A substances present in Mrs. J.'s serum in comparison with other group A people. Mrs. J.'s serum, together with sera from five other normal group A people, was serially diluted from 1/1 to 1/4,096. To one volume of each dilution was added one volume of a standard anti-A serum diluted 1/8 with isotonic saline. Each mixture was then left at 18° C. for 30 minutes and tested against a 2% suspension of fresh A_2 cells for a further 90 minutes, and the sedimented cells were examined microscopically for agglutination. The results obtained (Table II) showed that Mrs. J.'s serum, diluted 1/16, completely inhibited the anti-A agglutinins in this serum. This, then, gave a method of finding other bloods containing similar amounts of group-specific substances. For this investigation a standard anti-A serum was diluted 1/8, and to one volume of this was added one volume of each group A person's serum. After leaving the mixture at room temperature for 30 minutes a volume of 2% A_2 cells in saline was added and, after a further hour, examined microscopically for agglutination.

The test was performed on a series of 500 group A sera taken from blood-donor samples, and only one person was found who had comparable amounts of A substances in his serum. The results on this donor's (x/82372) serum are shown in Table III. The serum of this donor, whilst containing more A substances than that of the other 499 people investigated, did not contain as much as Mrs. J.'s serum. So far as was known the donor of this serum was a normal healthy person.

Mrs. J.'s cells were further typed and she was found to be A_2 and her Lewis type was Le(a−b+). From this it can be assumed that she was a secretor of A and H; but, unfortunately, saliva was never sent to us for confirmation of this. We examined her serum for H substances, using rabbit anti-H kindly supplied by Professor W. T. J. Morgan, and it will be seen from Table IV that Mrs. J. had a marked

TABLE IV

Subject	1	2	4	8	16	32	64	128	256	512
Cancer—										
Mrs. J. ..	–	–	–	–	–	w	w	(+)	(+)	(+)
Cancer—Mr. P.	+	+	+	+	+	+	(+)	+	(+)	(+)
,, Mr. W. ..	V	++	+	+	+	+	+	(+)	(+)	(+)
x/21625 ..	+	+	+	+	+	(+)	(+)	(+)	(+)	(+)
x/21627 ..	+	+	+	+	+	+	+	(+)	(+)	(+)
x/21630 ..	+	+	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)

excess of H substances in comparison with two other cases of cancer of the stomach and three normal blood donors. The serum plus rabbit anti-H (diluted 1/45) was incubated at 18° C. for one hour and then tested against group O cells for one and a half hours at 18° C. As a control the anti-H was incubated with saline instead of serum, and this mixture was found to agglutinate the O cells.

Mrs. J. died five days after admission, and necropsy, performed by Dr. R. Dodge at the Sheffield Royal Infirmary, revealed that she had a carcinoma of the cardia of the stomach with secondaries in various organs. Unfortunately, no further serum or other body fluids were available for investigation.

Discussion

So far as we are aware, the literature contains no reports of excessive amounts of ABO group-specific substances interfering with the determination of the ABO group. This may in part be due to the use of unwashed red cells for blood grouping and/or limiting the test sera to anti-A or anti-B, and/or unwisely determining the ABO group by examination of the red cells only. On systematic search of the sera of 500 group A bloods from donors we found one person who appeared to have excess of group-specific substances, but less than Mrs. J.

The association between cancer of the stomach and blood group A (Aird *et al.*, 1953) is a statement of fact—namely, that in persons with such cancers there is an excess of people who are group A. This observation and similar observations on associations between blood groups and disease pose two questions (Dunsford, 1957): (1) Does possession or absence of a particular red-cell antigen influence the proneness to a certain disease and in turn reduce the survival rate—that is, is there evidence of selection against people of a particular blood group? This selection may operate in other ways, such as affecting fertility (Allan, 1953), and result in balanced polymorphism. (2) Is any apparent association between blood groups and a particular disease not due to possession of a particular blood group, but due to genes responsible for that disease or proneness to the disease, occurring on the same chromosome as the gene for that particular blood group—that is, linkage? Such linkage has been reported in elliptocytosis (Chalmers and Lawler, 1953).

In view of the observations of Aird *et al.* and the questions these observations leave, when we knew the post-mortem findings on Mrs. J. we wondered whether: (*a*) the excess of group A specific substances was caused by or was a response to the carcinoma of stomach; or (*b*) the carcinoma was caused by Mrs. J. secreting an excess of A substances; or (*c*) there was no association between our observations and the cancer of the stomach.

The stomach is the richest source of ABO blood-group substances, containing ten or more times the

amount present in the erythrocytes. As yet the physiological function of these substances, which are complex mucopolysaccharides, is unknown. It seems reasonable to assume that there must be normal amounts of these substances in the various tissues and fluids in man and that if these are exceeded they may endanger life. In the case of Mrs. J. we were able to examine her serum only four days before she died. Had the amount of group-specific substances reached levels which were too great for survival? Had there been a continuous increase during the progress of the cancer? Glynn, Holborow, and Johnson (1957) demonstrated in one case of stomach cancer that the cancer cells stained specifically for A substance and the staining was deep. This would suggest that the cancer cells were either making or accumulating the group-specific substance and that more was present in the cancer cells than in normal cells. More work, using the technique of Glynn *et al.* (1957), would be valuable.

Attempts to find cases similar to that of Mrs. J. have so far been disappointing. We have examined the sera of 12 patients with carcinoma of the stomach for A, B, and H substances and none showed abnormal amounts of group-specific substances. There are at least two possible reasons for this. Firstly, none of these patients was near to dying; and, secondly, the sites of the cancer were not known with any accuracy. This latter may possibly be important, since it has been suggested that the site of the cancer may play an integral part in the association between blood groups and cancer. Balme and Jennings (1957) have reported that in gastric ulcer there is an excess of group O when in the body of the stomach. Billington (1956) also suggests that the association between ABO groups and gastric disease is concerned with the intragastric site. In Mrs. J. there was a carcinoma of the cardia of the stomach with extensive secondaries. Whether the primary or the secondary cancerous condition was responsible for the amount of group-specific substances is also open to speculation.

Others with better access to clinical material may be able to investigate the questions posed by our observations.

Summary

A patient dying with carcinoma of the stomach was found to have an excess of blood-group substance A in her serum. This was detected as the cause of difficulty in ABO grouping the patient.

Only one other person out of 500 tested was found to have comparable amounts of A substance.

The patient was also found to have an excess of H substance in her serum.

Whether the excess of A and H substances was the cause of, or was caused by, the cancer of the stomach is open to speculation. These findings are discussed in light of the association of blood group A and carcinoma of the stomach, and suggestions made for further work.

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ANTIBODY RESPONSE OF ADOLESCENTS AND ADULTS TO A BOOSTER DOSE OF POLIOMYELITIS VACCINE*

The response of children under 10 years of age to a third (booster) dose of British poliomyelitis vaccine has already been reported (Medical Research Council, 1957b). The majority of subjects responded well, with large rises in antibody titres to all three virus types. However, a few who had no detectable antibody to the type 1 component failed to produce the high levels to this type shown by the group as a whole.

The studies in adolescents and adults reported here have shown that this trend with type 1 was even more evident, although the results with types 2 and 3 were as satisfactory as in the younger children. An investigation has also been made to determine the effect on antibody response of increasing the amount of the type 1 component in vaccine and in varying the dose schedule in these age groups.

Methods of Investigation

Eighty-six public-school boys and 25 adult medical personnel, mainly students and laboratory staff, were bled before and 14 days after a 1-ml. booster dose of poliomyelitis vaccine given intramuscularly into the upper arm. The schoolboys, aged 13 to 18 years, were divided into groups of 34, 29, and 23 individuals, different groups being injected 6, 9, and 12 months after the initial course of two doses of vaccine. The adults received a booster dose 10 to 12 months after their initial injections. The antibody responses of all these subjects to the initial course of vaccination has already been published (Medical Research Council, 1958). The batches used in these subjects at that time were as potent as any American, British, or Canadian vaccine issued for general use in the United Kingdom and better than some that were regarded as satisfactory. The same batch of vaccine was used for the booster doses of each of the schoolboy groups, while different batches were used for the adults.

Sixty-nine medical personnel and 26 schoolboys participated in two investigations of the effect of increasing the type 1 component in vaccine. In the first, two vaccines, designated U and S_1, were used. U was a specially prepared trivalent vaccine, while S_1 consisted solely of U's type 1 component. Thus, the 1-ml. dose of S_1 had three times as much of this component as U. In the second experiment, vaccines H and S_2 were used. S_2 consisted of trivalent vaccine H together with an equal quantity of S_1 vaccine, 2 ml. of

*This report describes some of the results of investigations into the antigenic activity of poliomyelitis vaccines being undertaken by the Biological Standards Control Laboratory, Medical Research Council Laboratories, London, N.W.3.

Schoolboys were bled and injected by Dr. E. J. C. Kendall, Medical Officer of Epsom College, and by Dr. T. S. L. Beswick and Dr. J. O'H. Tobin, of the Biological Standards Control Laboratory.

Medical personnel in the special vaccine studies were bled and injected by Dr. R. L. Vollum (Oxford) and Dr. J. O'H. Tobin, and by Dr. A. M. Peach (London). The injection and bleeding of other adults were done by Professor Wilson Smith, F.R.S., Dr. P. Sneath, and Dr. A. Towers (London).

All the vaccines used in this study were prepared by the Glaxo Laboratories Ltd. under the direction of Dr. W. Wood.

Serum titrations were done in the Biological Standards Control Laboratory by Miss A. Petts and Dr. J. O'H. Tobin with the technical assistance of Miss O. Stanbridge.

The report was prepared by Dr. J. O'H. Tobin.

this combined vaccine being given at each injection. The primary antibody response in man indicated that the antigenicity of vaccine H was of the same order as those routine vaccines used in the main investigation reported here, while that of the U vaccine was about two-thirds of this potency. Thus the fortified vaccines S_1 and S_2 contained approximately two and three times as much type 1 component as vaccine H. Increasing the type 1 component of vaccine S_2 had no obvious effect on the response of subjects to the type 2 and 3 components, which were of the same order as those obtained with vaccine H.

All those who took part in these studies were "triple-negative" subjects, having no detectable antibody to any of the three types of poliomyelitis virus when they received their first dose of vaccine.

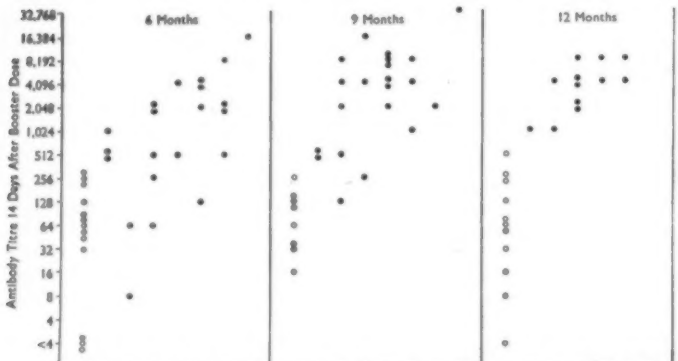

FIG. 1.—Type 1 antibody response in schoolboys to a booster dose of polio vaccine given 6, 9, and 12 months after the initial course of injections.

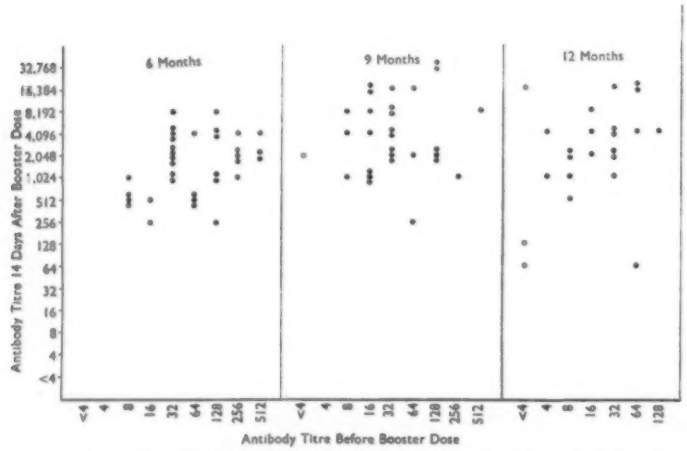

FIG. 2.—Type 2 antibody response in schoolboys to a booster dose of polio vaccine given 6, 9, and 12 months after the initial course of injections.

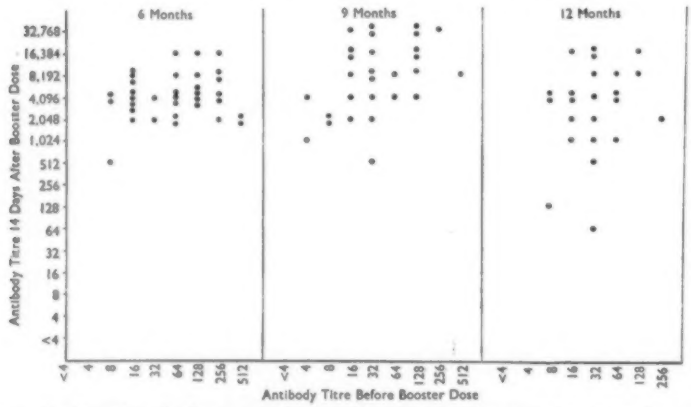

FIG. 3.—Type 3 antibody response in schoolboys to a booster dose of polio vaccine given 6, 9, and 12 months after the initial course of injections.

Antibody titrations were done in monkey - kidney-cell cultures by the method described previously (Medical Research Council, 1957a ; Perkins, Sousa, and Tobin, 1958), except that virus–serum dilution mixtures were held for six hours in an air incubator at 37° C. before being added to the cell cultures. With the exception of Fig. 5, each figure and table records titres found in tests of serum samples done at the same time in order to make comparisons more valid. In Fig. 5 the sera obtained during the first eight months of the investigation were titrated separately from the remainder.

Results

Antibody Response to the Booster Dose

The effect of the booster dose in schoolboys on the antibody levels to each of the three poliomyelitis virus types is given in Figs. 1, 2, and 3. As can be seen, the proportion of subjects who had no detectable antibody levels at the time of boosting (shown as open circles) was very much higher with type 1 than with the other types. Also, the left-hand columns in Fig. 1 show that the proportions without antibody—38%, 28%, and 48%—were not very different 6, 9, and 12 months after the initial vaccination. All those boosted had detectable type 3 antibody at this time, but four had no demonstrable type 2 antibody. The antibody level tended to fall more quickly during the first six months than subsequently ; in one year it had declined to about a quarter of the immediate post-primary inoculation value (Medical Research Council, 1958).

With all three types, those with demonstrable antibody gave a good response to the booster dose of vaccine. However, in the case of type 1 those without such antibody gave appreciably lower levels to this type. These levels were of the same order as were obtained in individuals with no type 1 but with pre-existing type 2 antibody, who had received only one dose of poliomyelitis vaccine (Table I).

The same pattern of response to the third dose was found in the adults who were boosted at 10 to 12 months ; those with no detectable type 1 antibody responded poorly compared with those

with antibody. The responses to types 2 and 3 were as satisfactory as those in schoolboys (Fig. 4).

The effect of delaying the booster dose is shown in Table II. With types 1 and 2 the geometric mean titres of the response of those with antibody were higher in the subjects boosted 9 to 12 months after the initial course than those injected after 6 months. With type 3 the mean titre of the 6-months group lay between the values for the 9- and 12-months groups.

TABLE I.—*Comparison of the Type 1 Antibody Response to One Dose of Vaccine in Subjects Without Type 1 Antibody, Who Had Either Induced or Naturally Occurring Type 2 Antibody*

	Induced Type 2 Antibody			Natural Type 2 Antibody
	6-months Group	9-months Group	12-months Group	
Geometric mean titre ..	34	69	72	55
No. of subjects	13	8	11	12

TABLE II.—*Geometric Mean Titres Obtained in Groups of Schoolboys 14 Days After a Booster Dose of Poliomyelitis Vaccine*

Type	Booster Dose given after		
	6 Months	9 Months	12 Months
1	840	2,670	3,460
2	1,550	3,802	2,851
3	4,420	6,460	3,020

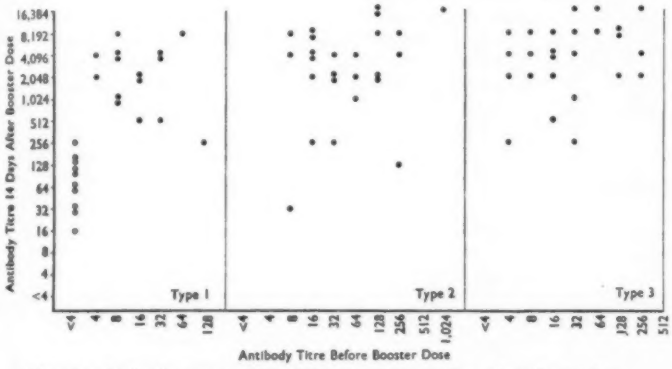

FIG. 4.—Antibody response in adults to a booster dose of polio vaccine.

Effect on Antibody Response of Altering the Dose Schedule and of Increasing the Type 1 Component in Vaccine

In an attempt to obtain a good booster response in all subjects, investigations were made into the effect of giving a fourth dose, or shortening the period between initial and booster doses in the hope that all would still have demonstrable antibody, and of increasing the proportion of the type 1 component in the vaccine.

Fig. 5 shows the response to the initial and to two booster doses, given to an individual who had antibody present at the time of the booster doses. After each dose the level of antibody to all types increased and the subsequent fall-off became slower. In Fig. 6 the type 1 antibody response of three subjects with no antibody to this type at the time of the first booster dose is shown. After this dose the response was little better than after the primary course, but a fourth dose nine months later produced a booster response in the two subjects with circulating antibody.

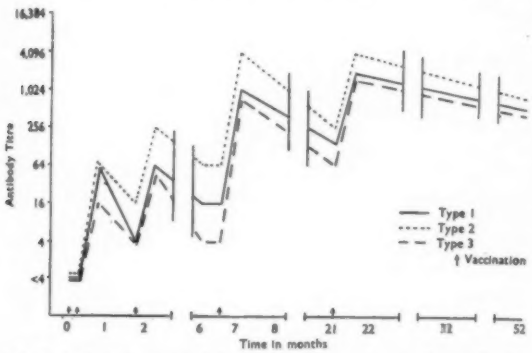

FIG. 5.—Effect of repeated doses of polio vaccine on the antibody level of a good responder to all components.

The time of onset of the response to a dose of vaccine was studied for types 1 and 3 in a small group of medical personnel with and without antibody to these types. Blood samples were taken at different times after injection and the percentage with detectable antibody is recorded in Table III. Those subjects with antibody, whether naturally acquired or induced, started to respond on the fifth and sixth days after injection, while, in those without any, antibody did not appear until on or after the seventh day whether they had been vaccinated previously or not.

TABLE III.—*Percentage of People Responding to Poliomyelitis Vaccine in Relation to Day of Inoculation. Types 1 and 3*

Type of Subject	Day				
	3	4	5	7	12–14
Natural antibody present ..	0 (10)	0 (15)	38 (13)	92 (12)	100 (15)
Vaccination antibody present >1/4	0 (7)	0 (4)	43 (7)	83 (6)	100 (8)
Vaccination antibody absent <1/4	0 (8)	0 (8)	0 (8)	50 (8)	100 (8)
Unvaccinated	0 (6)	—	0 (6)	33 (6)	100 (6)

Figures in parentheses show the number of subjects in each group.

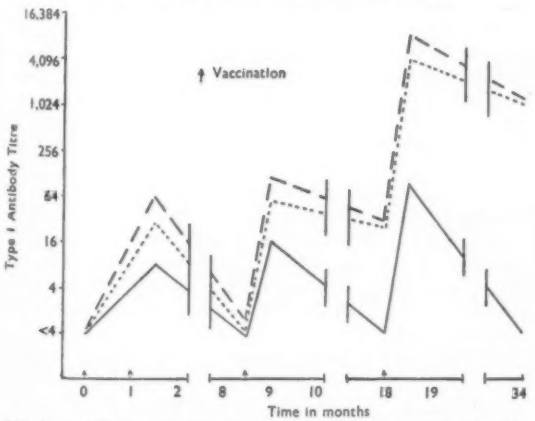

FIG. 6.—Effect of repeated doses of polio vaccine on the antibody level of three poor responders to the type 1 component.

The effect of increasing the type 1 component of the vaccine and of shortening the time between the initial and booster doses was studied, using vaccine U and the fortified vaccine S_1. The geometric mean type 1 titre obtained in a group of 22 " triple negative " adults given the initial two doses of S_1 a month apart and bled 14

days later was 60, compared with 21 in a similar group of 24 people given U vaccine. Three to four months later 12 people who had had S_1 and 17 who had had U were boosted with the same batch of routine commercial vaccine. At this time one of the S_1 subjects and five of the U subjects had no detectable antibody. The S_1 group, with a mean titre of 1,820, responded better to this third dose than the U group with a mean titre of 263. These results are illustrated in Fig. 7. The

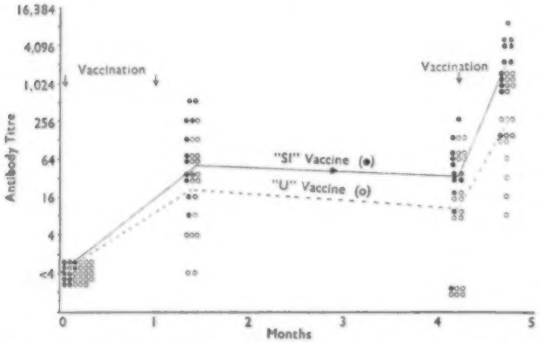

FIG. 7.—Effect on the type 1 antibody response in adults of increasing this component of polio vaccine.

subjects with no antibody at this time responded in a similar manner to the schoolboys and the other adults who had lost theirs, none having a titre of more than 1/128 after their third dose. The mean response of the S_1 and U subjects who had antibody when the three- to four-months booster was given was 960, compared with 2,050 in the adult group boosted 10 to 12 months after the initial vaccination course.

The effect of the addition of still more of the type 1 component to vaccine was shown by the primary response of individuals given two doses of vaccine H and of the fortified vaccine S_2. The geometric mean titre obtained for type 1 in a group of 21 "triple negative" individuals was 151 for S_2 and in a group of 18 such people was 32 for H, the lowest individual responses being 1/16 and 1/4 respectively. This study is not yet complete, as the booster effect on people receiving these two vaccines has not yet been determined. However, six months after the initial course all of the 13 S_2 subjects so far bled had antibody levels of 1/16 or more to type 1.

Discussion

The use of a third injection of poliomyelitis vaccine some time after an initial course with a view to eliciting a booster response is probably the best method of assessing the efficacy of the vaccine in inducing immunity. This is especially so in a disease in which the organization of repeated field trials is out of the question owing to the large number of individuals needed to give a satisfactory answer.

The results obtained with a booster dose of vaccine in adolescents and adults, who before their initial vaccination had no antibody to any of the three poliomyelitis virus types, have shown certain shortcomings in even the best commercial vaccines at present available. As has been noted above, the vaccines used in this investigation were as potent as any that had been tested in the Biological Standards Control Laboratory and better than many that have been used in the field generally.

Thus it appears that after three intramuscular doses the best commercial poliomyelitis vaccines can be considered to furnish a satisfactory immunity in adolescents and adults to type 2 and 3 infections for some time. However, with type 1, about a third of those in these age groups injected with the two doses will not be protected even for a few months, and after the third booster dose will probably not be immune to this type for more than a year or two. With present commercial vaccine a fourth dose will thus be necessary if a booster response and long-lasting immunity to all three types is to be obtained in more than two-thirds of the susceptible older people vaccinated. So far, no adverse effects have been reported from repeated doses of poliomyelitis vaccine (Salk, 1958).

In the age groups studied, the subjects fell into two groups as far as the antibody response to type 1 was concerned. After the initial course about 60–70% produced antibody, which continued to be detectable for at least a year, while the remainder had lost whatever they had produced initially within six months. Administering the third dose three to four months after the primary course did not decrease the proportion of poor responders or the number who lost their induced antibody to this type. It would seem that an adequate basic immunity is not laid down by the primary course in some subjects, and these will not respond satisfactorily to a third dose irrespective of when it is given. Salk (1955) has shown that too short an interval between these doses tended to inhibit the booster effect, which increased as this interval was lengthened. He suggested a minimum of seven months between them, and the results reported here would support this finding and indicate that it is probably better to wait and give the third dose 9 to 12 months after the initial course. If the third dose is delayed longer than this it is possible that some of those with no type 1 antibody will have lost their type 2 antibody as well. Since the presence of type 2 antibody enhances the response to the type 1 antigen (Russell, 1958), its absence would presumably decrease still further the chances of a satisfactory response to type 1 after a third dose.

However, it may not always be advisable to wait 9 to 12 months before giving the booster dose, because of the imminence of the poliomyelitis season, during pregnancy, or for some other reason. If there is an enhanced risk of contact with poliomyelitis it may sometimes be better to give the third dose even as early as three to four months after primary immunization. If a better type 1 component is produced a reasonable response to a booster dose can occur at this time, as can be seen from the results in subjects who had been immunized previously with the fortified vaccine S_1 (Fig. 7). The lack of any increase in the booster response with time with the good type 3 antigens used in these studies (Table II) may indicate that with more potent vaccines the period between the primary and booster injections may be more elastic than would seem to be the case with the present ones.

Although it has been suggested that a sensitized condition in the absence of circulating antibody is all that is needed for immunity, there is no evidence that this state is in fact protective. In diphtheria the booster response to antitoxin in people with very low antibody levels may not be quick enough to stop clinical disease (Medical Research Council, 1950). The time of the antibody response in vaccinated subjects was the same as in unvaccinated controls when attenuated poliomyelitis virus was fed by mouth (Sabin, 1957). As has been

shown here, the antibody response to formalinized vaccine occurred no sooner in those vaccinated people without detectable antibody than in normal subjects, irrespective of the final antibody titre reached. In two-thirds of those subjects with antibody no rise occurred before the sixth day.

The geometric mean titre obtained after the initial vaccination course in those schoolboys who responded well to a booster of type 1 was 1/85, while in those who had lost antibody it was only 1/10. Vaccines S_1 and S_2, which contained respectively two and three times the usual amount of type 1, produced mean primary responses of 60 and 151 to this type in the groups vaccinated with them, as compared with a mean of 32 produced by routine vaccine H (unpublished results). Thus, a mean titre of 1/85 in a group of people may give some indication of the minimum antibody level following primary immunization which is required to ensure a good booster response to a subsequent dose of vaccine. To obtain this level in adolescents and adults a threefold increase in the potency of the type 1 component would seem to be necessary in vaccines of the quality used in these studies. With some other commercial vaccines as much as a tenfold increase might be necessary to ensure an adequate long-term immunity to type 1 after three doses.

The increase in the type 1 component which would appear necessary from the studies reported here could be obtained by doubling the potency of this type in the best vaccine now being manufactured. The present schedule of two doses of 1 ml. for the primary course of immunization should then be sufficient to produce an adequate response in those children who do not react satisfactorily to present vaccine, while two 1.5-ml. doses should be adequate for adolescents and adults; 1 ml. should be sufficient for the booster dose in all age groups.

However, before it can be shown conclusively that such an increase in antigenicity will be effective, the results of a booster dose in the people receiving S_2 vaccine must be determined. But Salk (1958) has clearly shown that the degree of the booster response is proportional to the potency of the vaccine used for the primary inoculation course. Our results with vaccines S_1 and U would support this finding, although in our case the booster dose was given too soon for the optimal response to be obtained. If an increase in potency does not enable all subjects to continue with circulating antibody until the booster dose is given and then produce a good response to it, a fourth dose—with its accompanying administrative difficulties—will be necessary if the long-term immunity, as is obtained in tetanus and diphtheria, is desired. Otherwise, attenuated live virus vaccines will have to be considered either alone or in combination with killed vaccine (Paul *et al.*, 1957).

Summary

A booster dose of poliomyelitis vaccine given to 111 adolescents and adults 6 to 12 months after primary immunization produced a good response to types 2 and 3. At this time all these subjects, except four, still had detectable antibody induced by their initial course of vaccination. With type 1 a third had lost their antibody, and these responded poorly compared with those in whom it was still present. In these poor responders to type 1 a fourth dose appeared to produce a booster response to this type.

It is probable that in the age groups studied at least a threefold increase in the amount of type 1 antigen in poliomyelitis vaccine will be necessary to give satisfactory antibody responses after three doses in all subjects.

Thanks are due to the headmaster and boys of Epsom College and to all the other people who so kindly co-operated in this study, and also to the Ministry of Health for the supply of some of the vaccine used in it.

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MANAGEMENT OF POLIOMYELITIS*

BY

W. RITCHIE RUSSELL, C.B.E., M.D., D.Sc. F.R.C.P.

Director, Department of Neurology, United Oxford Hospitals

In 1947 there was a sudden increase in the cases of poliomyelitis in this country from an annual incidence of 1 or 2 per 100,000 to over 10 times this rate. This led to a great increase in interest in the disease. Little money was available to support research on poliomyelitis at the time, but, in spite of that, many careful clinical studies were carried out in various parts of the country.

It was inevitable that our chief efforts should be directed towards the clinical problems of recognizing the disease and of saving life. Lord Nuffield's inspired provision of 800 iron lungs 10 years previously provided a nucleus of equipment which saved many lives; but it was evident that improved apparatus was needed, and the Ministry of Health set up a Breathing-Machine Working Party, which has contributed much to the present satisfactory position. After the exceptional outbreak of the disease in Denmark in 1952 (Lassen, 1953), the Ministry encouraged the establishment of at least one special respiration centre in each region, to which problem cases could be transferred and at which the latest machines would be available for treatment.

At the same time it became obvious that notifications of the non-paralytic form of the disease were unreliable, and since 1950 the notifications of paralytic poliomyelitis in England and Wales have been carefully and, I think, accurately separated from everything else. This was an important step, one which was long ago adopted by Denmark, and it has made the figures for England and Wales among the most reliable and useful in the world in regard to the all-important paralytic form of the disease.

Case Fatality Rates

One of the most important consequences of this new type of notification is that the fatality of the paralytic cases can be compared from one year to the next

*Read to the Section of Medicine at the Annual Meeting of the British Medical Association, Birmingham, 1958.

without the confusion caused by varying notifications of meningeal states as non-paralytic cases.

It has on occasion been suggested that the case fatality rate in poliomyelitis varies greatly from one outbreak to the next, and in fact this variation did occur 25 or more years ago. In more recent years, however, since the methods of saving life have been developed one by one, the case fatality rate has become slowly reduced in the U.S.A. and other countries, and, what is more, the paralytic case fatality rate is now apparently almost uninfluenced by the nature of the epidemic. Thus in most outbreaks about 30% of all paralytic cases are what Lassen (1953) calls "life-threatening," and 25 years ago 20 to 30% of paralytic cases would be fatal. Since then, however, the figure has steadily dropped, and should now be about 5 per 100 paralytic cases.

Figs. 1 and 2 show these dramatic changes, and there is, I believe, no doubt at all that this advance is due to the improved methods available for saving life. Thus in 1957 there were in England and Wales about 3,200 paralytic cases with 226 deaths—a case fatality of 7.1%. With the methods available 20 years ago there would probably have been about 600 deaths in these cases — about three times the rate that actually occurred.

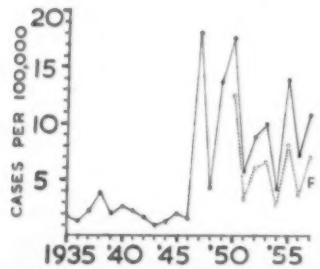

FIG. 1.—Incidence of poliomyelitis per 100,000 of population of England and Wales, 1935-57. The dotted line (P) gives the number of paralytic cases.

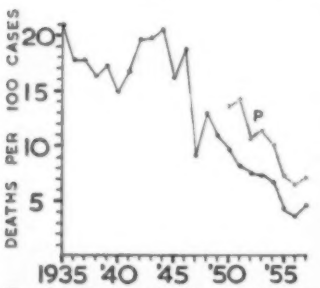

FIG. 2.—The case fatality rate (deaths per 100 cases) for England and Wales from 1935 to 1957. The dotted line (P) gives the rate for paralytic cases.

This is a very gratifying state of affairs, but it also brings special problems; for inevitably there also is an increase in the number of severely disabled persons whose lives have been saved, and who provide special problems as regards prolonged care and rehabilitation. What, then, are these advances that have led to this striking reduction in fatality rate?

In the first place clinicians will agree that in the old days most of the deaths were caused by respiratory insufficiency, and the newer methods save many of these cases.

Management of Respiratory Paralysis

Acute poliomyelitis is usually handled in isolation hospitals, the staff of which are subjected to very great strain when sharp local outbreaks occur. The first requirement is to recognize the cases in which life is threatened and to ensure that the most experienced medical and nursing staff are made available to devote sufficient time to their supervision and treatment. The remaining 60 to 70% are never in danger of losing their life, and during epidemics they should be cared for by the less experienced of the medical and nursing personnel.

The life-threatening cases are therefore our chief interest, and these fall into clear groups, each of which requires a special type of treatment. First, there are the common cases in which the muscles of respiration are weakened but the patient is fully conscious and the bulbar muscles are unaffected. For these the tank type of respirator supplies the artificial respiration required, and this should be used to rest the weak muscles long before the breathing is seriously embarrassed. The modern type of tank respirator, such as the excellent one designed in the Birmingham Region by Captain Smith-Clark,* is more comfortable than a hospital bed, and a skilful team can transfer a patient to it without either physical or psychological upset. For spinal forms of poliomyelitis the tank respirator is admirable, but some patients adapt themselves better to it than others for a number of reasons, and sometimes secretions form in the airways and make a tracheotomy necessary.

Secondly, the pure bulbar cases are those in which the muscles supplied by the brain-stem nuclei become paralysed, and for these the life-threatening situations generally depend on whether or not the patient can swallow safely without danger of inhalation. Early recognition is of special importance and must often be made by the general practitioner. The adult can usually describe his symptoms, but the child just refuses to eat or drink. Often, however, an audible bubbling of secretions in the throat makes the diagnosis clear. Sometimes the patient is unconscious, and coma plus a "death rattle" in the throat make matters seem to be far worse than they really are. Indeed, bulbar cases, in which the patient is unconscious early, often make an apparently complete recovery if the airways are properly looked after in the acute stage (Russell, 1956).

These cases provide special difficulties in that it may be difficult to distinguish between stupor caused by encephalitic lesions in the brain stem and stupor caused by hypoxia. When the respiratory centre is involved in the encephalitic process respiration may be inadequate even though there is no paresis of respiratory muscles. In most bulbar cases the secret of success rests with taking care of the airways. The skilled exploitation of postural drainage now saves many lives that were formerly lost, but it is desirable to be prepared to do a tracheotomy at very short notice. In general, however, many cases of the once dreaded bulbar type of poliomyelitis have become the type that is most to be welcomed by the special unit, for the extent of physical recovery is usually very good if life can be maintained during the acute stage.

The proper nursing of this group of cases has probably done more than anything else to reduce the fatality rate, but the general practitioner should, as soon as he recognizes the condition, turn the patient into the prone position and raise the foot of the bed. Transfer to hospital must be carefully supervised with semi-prone lying on the stretcher, and portable suckers should be available to deal with secretions or vomit. The patient should not be allowed to lie supine on a stretcher or bed —the inhalation of a single mouthful of vomit often causes lung changes which are inevitably fatal. The special respiration centres are often able to send a nurse

*Manufactured by the Cape Engineering Co. Ltd., Warwick.

and doctor with the ambulance to increase the safety of moving these patients.

When both throat and respiration are paralysed the tank type of respirator can be used only if a tracheotomy is done, preferably with a cuffed tube, which prevents secretions from passing from the pharynx into the trachea.

Intermittent Positive-pressure Respiration

Some of the American special centres became very expert at handling these cases in this way, but in Great Britain most of us have adopted the Copenhagen method of supplying artificial respiration through the tracheotomy tube by intermittent positive-pressure ventilation (I.P.P.R.) From the physiological point of view these two alternatives are much the same, but the wave form is easier to control with I.P.P.R., and frequent changes of posture with chest physiotherapy are more easily and efficiently achieved with I.P.P.R. and the patient on a tilting bed than is possible in a tank respirator. Fig. 3 shows the pressure changes and air

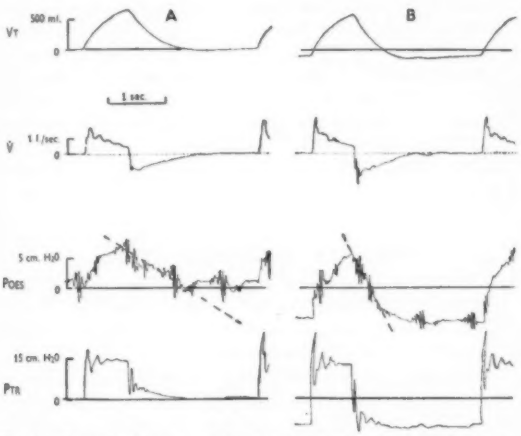

FIG. 3.—Records from a paralysed patient receiving I.P.P.R. from a Radcliffe pump. Tidal volume (VT), air flow (V̇), oesophageal pressure (POES), and tracheal pressure (PTR) are shown first with positive pressure only (A), and, secondly, (B) with the addition of a negative-pressure phase throughout the expiratory phase of the pump.

flow which occur during I.P.P.R. with a Radcliffe respiration pump,* and experience has shown that this form of artificial respiration can be maintained for many months, and indeed years, without serious difficulty.

The I.P.P.R. pumps are specially convenient for transporting patients, and a safe airway can be provided for a few hours by intubation by endotracheal tube. Thus the Radcliffe pump can be run on one car battery for a period of 24 hours, and many patients are now flown to this country from Africa or Asia on I.P.P.R.

At first sight it may appear that all this effort to save life will soon be no longer needed after vaccination programmes have eliminated the disease, but experience has shown that the methods developed in recent years are of value also in saving life in other diseases. Of these, the most important are acute infective polyneuritis, tetanus cases under treatment with full curarization, myasthenia gravis, respiratory insufficiency after thoracic operation, and certain chronic diseases of the heart and lungs. It seems, therefore, that the special efforts made in recent years with regard to poliomyelitis will pay dividends in regard to several other medical conditions.

*Manufactured by H. G. East and Co. Ltd., 37, Oxford Road, Cowley, Oxford.

Care of Muscles

The ways of caring for limb and trunk muscles in the acute stage of disease still arouse a good deal of controversy, and many different methods are being observed. Few, however, will disagree with the view that in the life-threatening cases any type of splinting gets in the way. Our own experience in Oxford and Stoke Mandeville is that in these cases the position of the body has to be changed through 90 or more degrees every two hours, and if at this time one or two minutes are devoted to gentle passive movements of most joints, and if this routine is begun at the onset of the illness, the tight and painful muscles we so often used to see rarely develop and are never troublesome. We rarely use hot packs, as they also get in the way and distract attention from more pressing matters.

Complete avoidance of voluntary movement in the acute stage seems to be desirable so far as it is practicable; but after two to three weeks—what then? Some still advocate long weeks of complete rest with emphasis on keeping the weak muscles relaxed, but the weak muscles should not be allowed to shorten or they will become damaged and weakened when normal range of movement is resumed. This occurrence may lead to the weakening of a supported muscle after splints are removed. When this happens the removal of the splint may be blamed, whereas the real cause has been over-prolonged splinting of weak muscles in a shortened position.

Our experience favours plenty of freedom for voluntary movement within two to three weeks of the acute stage, but it is difficult to establish the relative merits of the various methods in use.

The physiological mechanisms whereby paretic muscles increase steadily in strength for several months after the acute stage raise many interesting problems which require reassessment in relation to the latest knowledge of the organization of the spinal cord cells, but these rather academic matters cannot be considered further at present.

I am greatly indebted to Dr. John Spalding and Dr. Lionel Opie for the record in Fig. 3 (see Opie, Spalding, and Stott, 1959).

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At the beginning of the year the National Association for the Prevention of Tuberculosis changed its title to the Chest and Heart Association, and its journal, formerly known as the *N.A.P.T. Bulletin*, now follows suit. In the February issue of the *Chest and Heart Bulletin*, the DUCHESS OF KENT, the president of the Association, Sir JOHN CHARLES, Sir CLEMENT PRICE THOMAS, and Dr. SHIRLEY SMITH pay tribute to the usefulness of the journal under its old title and wish its new self an equally useful and distinguished life.

SOME DIAGNOSTIC PROBLEMS SURROUNDING POLIOMYELITIS*

BY

J. F. GALPINE, M.D., F.R.C.P.Ed., D.P.H.

Medical Superintendent, Whitley Hospital, Coventry

In this paper reference is made to three problems in the recognition of poliomyelitis that are topical. Firstly, the diagnosis of non-paralytic poliomyelitis and its relationship to similar syndromes mainly of virus origin and often referred to as "aseptic meningitis"; secondly, the need to distinguish the paresis of so-called "benign myalgic encephalomyelitis" from paralytic poliomyelitis; thirdly, the existence of polioencephalitis unaccompanied by paralysis.

Recognition of Non-paralytic Poliomyelitis

The term "non-paralytic poliomyelitis" refers to the so-called major illness or nervous phase of poliomyelitis when this develops without the supervention of paralysis. In outbreaks of poliomyelitis one case of this type occurs for every two or three cases with paralysis. Looked at in another way, non-paralytic poliomyelitis is a mild meningitis of viral origin and is an example of a group of similar illnesses to which the term "aseptic meningitis" is often applied, especially when the aetiology is in doubt.

Viral meningitis cases have a cerebrospinal fluid of clear or near-clear appearance with a pleocytosis often between 10 and 500 or so cells per c.mm., but sometimes reaching 2,000 or over, with very variable proportions of polynuclear cells and lymphocytes, but over a series often leaning to lymphocytic preponderance. Perhaps half the cases show an increase of C.S.F. protein usually to less than 100 mg. per 100 ml., with normal sugar and chloride values.

Although sporadic cases of aseptic meningitis may be due to poliomyelitis infection they may also be due to the virus of mumps or of benign lymphocytic choriomeningitis, or may occasionally accompany glandular fever. If, on the other hand, they occur in large numbers, with an absence or near absence of paralytic cases, they are more likely to be due to one of the Coxsackie viruses or, as has been appreciated more recently, one of the so-called E.C.H.O. viruses, infection by which may sometimes be accompanied by a rubelliform rash (*British Medical Journal*, 1957). These two virus groups, together with the poliomyelitis viruses, are all very similar in their physical properties and form a larger group, to which the term "enteroviruses" is beginning to be applied (*British Medical Journal*, 1958). Whilst the virologist can assist by performing serological tests for mumps and lymphocytic choriomeningitis, and by isolating poliomyelitis virus from excreta, other relevant virological investigations are not yet available routinely.

Certain non-viral conditions need to be distinguished from aseptic meningitis of viral origin. In anicteric leptospiral meningitis, usually due to *Leptospira canicola* infection, there are similar findings in the C.S.F., but the correct diagnosis is suggested by the usual occurrence of conjunctival suffusion and some degree of nephritis (Ramsay, 1955); laboratory investigations, especially for the development of antibodies, may confirm suspicion. It is especially important to distinguish aseptic meningitis from tuberculous meningitis with its steady clinical deterioration and increasing drowsiness, cranial palsies in advanced cases, wider C.S.F. changes, including the presence of acid-fast bacilli, and the frequent concurrence of other tuberculous manifestations. Aseptic meningitis may occasionally have to be distinguished from post-infection encephalitis, partially treated bacterial meningitis, aseptic meningeal reaction to an adjacent septic focus such as extradural abscess or venous sinus thrombosis following mastoid infection, and the rare acute syphilitic meningitis. In some districts it may also be necessary to bear in mind tick-borne virus infection of the Russian spring/summer encephalitis/louping-ill group, illness from which may be non-paralytic or paralytic (Likar and Dane, 1958).

The diagnosis of non-paralytic poliomyelitis being so often uncertain, many cases of aseptic meningitis due to viruses other than poliomyelitis have in the past undoubtedly been included in the poliomyelitis figures; only paralytic cases should therefore be counted in comparing rates (Medical Officers of Schools Association, 1948), and since 1950 this has been made possible by requiring notifications of poliomyelitis to state whether the disease is of the paralytic or non-paralytic form. It is also apparent that in situations where the aetiology of a sporadic case of aseptic meningitis is completely uncertain it is unfortunate if a speculative label of "non-paralytic poliomyelitis" becomes attached to it with its possibilities of needless public alarm.

Benign Myalgic Encephalomyelitis

Reference may now be made to "benign myalgic encephalomyelitis," which is the term suggested by the *Lancet* (1956) to denote a type of neurological disease which appears to have occurred in widely different parts of the world in recent years and which does not classify under any of the previously established entities. It is "benign" in the sense that there seems to be no appreciable mortality (although in some cases sequelae may persist) and "myalgic" in the sense that muscle pain is frequent rather than invariable. Other terms which have been used are "epidemic myalgic encephalomyelitis," "acute encephalomyelitis—cause unknown," "Icelandic disease," and in the Royal Free Hospital it was nicknamed "the pest."

In Coventry attention was aroused in the summer of 1953 when about a quarter of the staff (13 in number) coming into contact with poliomyelitis patients in the infectious disease unit in Coventry developed an illness in which all but one of those affected showed some degree of paresis often associated with a peculiar jerking quality of volitional movement (Macrae and Galpine, 1954). Slight pyrexia occurred in about half the cases, also headache, drowsiness, and discomfort, pain, and even rigidity in the neck and back. Tendon reflexes, though largely unaffected, were occasionally disturbed, with a tendency to early depression and later exaggeration. Muscular aches and paraesthesiae were complained of, and four of the affected staff had areas of hypoaesthesia or hyperaesthesia unrelated to segmental or peripheral nerve distribution. Disturbance of micturition occurred in four cases. In convalescence several complained of inability to concentrate mentally. The cerebrospinal fluids gave almost wholly normal

*Read to the Section of Medicine at the Annual Meeting of the British Medical Association, Birmingham, 1958.

findings. Wasting was either absent or, if present, not commensurate with the paralysis, from which there was a marked tendency to recovery earlier and more completely than would have been expected in poliomyelitis.

Extensive laboratory investigations failed to reveal any evidence of poliomyelitic infection, but electromyographic abnormalities with a discrete pattern of action potentials on attempted voluntary movement were found in three of the staff cases (J. Shulman, 1953, personal communication). Amongst a considerable number of patients admitted from Coventry and district as cases of paralytic poliomyelitis in the same season, an increasing proportion, most of them female, showed early recovery from their paralysis and a normal C.S.F. In many of the patients, therefore, the illness paralleled that in the nurses.

A similar outbreak affected some of the nursing staff of the Middlesex Hospital in 1952 (Acheson, 1954), but the largest outbreak recorded in this country occurred in the Royal Free Hospital in 1955, when nearly 300 members of the staff were affected. Malaise, lassitude, sore throat, enlarged cervical glands, and gastro-intestinal disturbances occurred at onset, and later symptoms included cerebral irritation, depression, cranial nerve disturbances (including vertigo), motor and sensory disturbances in the limbs, minor disturbance of reflexes, and sometimes intense muscle spasm (Dimsdale, 1957). As in Coventry, electromyographic abnormalities were found, and these were characterized on volitional movement by a reduction in motor unit potentials that individually were often polyphasic; in addition a peculiar grouping of potentials was seen, constituting a novel feature of obscure origin. The electromyographic pattern suggested involvement of the motor unit at cord level without, however, the electrodiagnostic signs of lower motor neurone degeneration common to such diseases as syringomyelia and anterior poliomyelitis (Richardson, 1956). Sporadic cases of a similar illness admitted in 1955 from the local population to the infectious diseases unit of the Royal Free Hospital formed the background to the staff illness (Ramsay and O'Sullivan, 1956), and further cases were admitted in 1956 and 1957 as reported by Ramsay (1957), who stressed the occurrence of sequelae, sometimes neurological, but characteristically including proneness to fatigue and emotional lability.

In Coventry seven further cases of the syndrome were admitted in 1956 (Galpine and Brady, 1957) and three more were seen in 1957 during a time of high poliomyelitis incidence locally. The most typical of the latter was the following case.

A woman of 29 had backache, general aches, and very marked lassitude for four days, followed by a feeling of instability and aching in her legs, worse after exertion. Her doctor found marked general weakness in her left leg, with normal reflexes and a temperature of 99° F. (37.2° C.). In hospital her left hamstrings were found to be painful on stretching and there was diffuse tenderness in the muscles of the left leg. This leg could with difficulty be lifted clear of the bed and then only after a characteristic pause for concentration. Voluntary movements of the left foot were very weak and restricted, and the left ankle-jerk appeared slightly reduced. Blunting of sensation to touch and pain and to vibration and position was found in the left ankle and foot. She complained of flickering sensations in the muscles of her weak leg. There was also slight weakness and aching on exertion in the left upper arm. The C.S.F. was normal. The patient was discharged home to have out-patient physiotherapy after two and a half weeks in hospital, by which time sensation had very largely recovered and she walked fairly well, although dragging her left foot if she attempted to hurry. When seen seven months later her disability was minimal, but there was still slight weakness in the left foot and she complained of early tiring and aching in the left leg with a tendency for the left foot to turn in at such times.

Whilst the aetiology and pathology of this condition are, as yet, unknown, an underlying consistency exists in the versatile clinical picture and there seems good reason to suppose that it is a specific type of encephalomyelitis. Cases of this type, especially if occurring sporadically in the general population, may attract other and more familiar labels—for example, "paralytic poliomyelitis" and "hysteria."

Polioencephalitis

Finally, there is the problem of polioencephalitis. Although paralytic poliomyelitis has a reputation for not usually affecting cerebration, the occurrence of widespread paralysis in a patient, especially if including bulbar paralysis, is not infrequently accompanied by cerebral disturbance, either biochemical in origin and associated with respiratory inadequacy—a very important group—or truly encephalitic. In a description of his own attack of paralytic poliomyelitis made by a medical author (Personal Papers, 1953) the section on mental state includes the following:

"I was much troubled by flight of ideas; a succession of confused and unrelated thoughts sped through my mind so rapidly that I was unable to seize and hold any one of them. This experience was particularly frustrating and annoying at night, preventing any sustained thought or contemplation during many sleepless hours. Nevertheless it had its compensations, for the serious nature of my illness caused me relatively little apprehension during the early days. . . . During this period of confusion I had fantastic daydreams. My favourite was one in which I lay couched in my own medulla watching the outfall of nerve-cells from my nucleus ambiguus, an experience characterized by the complete absence of any affective element. For several days I was unable to appreciate the size and arrangement of my cubicle: at night, for instance, it expanded to an enormous room in a mythical house on the South Downs, or contracted to the box-like compartment where the stable-lad sleeps at my daughter's riding-school. In the confusion resulting from this uncertainty as to my whereabouts I was prone to get out of bed at night. . . . It was . . . about a month before my mental state was completely normal."

Whilst the foregoing may be presumed to refer to the encephalitic component of an attack of paralytic poliomyelitis classifiable and notifiable as such, the position is less clear if encephalitis occurs without paralysis but along with evidence—epidemiological or virological—that the poliomyelitis virus is at work. This kind of thing used to be notifiable separately as polioencephalitis before 1949, but in that year regulations were made abolishing this and including the condition in the term poliomyelitis. This is because it was felt that if polioencephalitis exists as a separate disease it is difficult to describe and to distinguish from other forms of encephalitis. There have, however, been a few reports of the isolation of poliomyelitis virus from cases diagnosable as encephalitis. For example, evidence of infection with poliomyelitis virus was present in seven out of nine cases of encephalitis-like illness seen during a poliomyelitis epidemic in Sheffield in 1955 (Snell *et al.*, 1957).

In Coventry in 1957, a year in which 141 paralytic cases were admitted to the local isolation unit, six cases of acute encephalitis-like illness were admitted at the height of the poliomyelitis incidence, with a good recovery in each instance. In two of them the faeces were examined for poliomyelitis virus, and type 1 virus was found in both. All six were pyrexial, with meningeal signs in all except one and C.S.F. changes consistent with poliomyelitis in all save one other. Two of these patients were girls aged 8 and 3 years who presented fully conscious but with ataxia—in one of them limited to the left arm and leg. Another girl of 3 was also conscious but exceedingly irritable, and showed violent generalized clonic spasms especially affecting her eyes, face, and head. Any attempt to sit her up caused her to scream and the movements to increase, but when she slept the spasms disappeared. Two boys aged 6 and 10 presented in stupor ; one of them lay quietly on his side, but if disturbed resisted violently with extreme hyperpnoea and the development of carpopedal spasm in a matter of minutes—which passed off just as quickly when he was left alone. The sixth case was that of a business man of 35 who had episodes of confusion in which he performed ridiculous acts—for example, trying to post a bundle of his belongings in the ward kitchen. It is a reasonable clinical supposition that "non-paralytic" cases of the above type occurring in the midst of a poliomyelitis epidemic are in all probability examples of "polioencephalitis."

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St. Luke's Printing Works in Old Street, London, which was built as a hospital in 1784, was sold in January by the Bank of England for over £1m. Charles Dickens, who visited the hospital in 1852 (see *Journal*, 1951, **2**, 1518), describes how it was founded as a new hospital for the insane by "half a dozen gentlemen" who were perturbed to see that the hospital at Bethlem was incapable of receiving and maintaining the great number of "melancholy objects of this sort who apply for relief." The hospital's first home was a building called The Foundry (in what is now Tabernacle Street), where cannon had originally been cast and where later John Wesley preached. In 1784 George Dance, the architect, designed the new St. Luke's, the building in Old Street, which opened two years later. Since Dance's first important work had been the rebuilding of Newgate Prison it is hardly surprising that the new hospital had a massive and rather forbidding appearance. The Old Street building ceased to be a hospital in 1917, but during its long life it admitted 25,569 patients, of whom 11,077 were discharged cured. The hospital's name and purpose is perpetuated in the St. Luke's Woodside Branch of the Middlesex Hospital. In the nineteenth century the hospital's visitors included, besides Charles Dickens, Charles Lamb, who was one of its governors, and Mrs. Elizabeth Fry.

EPIDEMIOLOGY OF POLIOMYELITIS*

BY

G. W. A. DICK, M.D., D.Sc., F.R.C.P.Ed.
The Queen's University of Belfast

It is now well established that there are three types of poliovirus—types 1, 2, and 3—and that type 1 is responsible for about 80% of all paralytic infections. Although these types are immunologically distinct there is evidence which indicates a degree of relationship between them, and this may be of importance clinically. It must be remembered that paralysis is not a common outcome of infection with a poliovirus, for, as is well known, infections with all types of poliovirus are a common experience ; usually there is an alimentary infection which is clinically either inapparent or unrecognizable. It has been shown that infections at a clinical or subclinical level generally result in resistance to further attacks.

Transmission of the Virus

The virus is spread by person-to-person contact, and children are probably the most important disseminators of virus in the community. The reason for this is that virus multiplies better in the alimentary tract of children than of older persons, and the children therefore excrete much greater quantities of virus and are thus more infectious.

There is no evidence that animals or birds enter into the natural history of the disease. Recently there was a report from the West of Scotland which suggested that budgerigars might play a part in the transmission of the virus. Dr. D. S. Dane and I have so far been unable to infect budgerigars with any of 12 different strains of poliovirus.

After infection, virus is found in the throat secretions of a proportion of individuals for a few days and in the faeces for weeks or months. In addition to the fact that children excrete more virus than adults we have also some evidence suggesting that there is a family pattern of virus excretion. Thus the children of some families seem to excrete more virus than those of other families. There appear to be "hot" families in whom the virus multiplies well and "cold" families in whom virus multiplies poorly. This familial susceptibility may be of importance in the pathogenesis of the infection and also in the spread of virus in the community. The precursor of paralysis is viraemia, and it may be that, in those families in whom virus multiplies well because of its greater multiplication in the gut, there is more chance of the virus getting into the blood stream and thence to target areas in the C.N.S. where the damage is done. This does not mean, of course, that everyone who gets viraemia will become paralysed. The time relationship between the pathogenetic events and the clinical picture is shown in Fig. 1.

This represents the sequel of events in a paralysed child. Essentially the same picture occurs in the asymptomatic infection but with little or no invasion of the C.N.S.

If a child becomes infected it is a common experience for all members of the family to be also infected. This occurs whether or not any of the family is showing signs or symptoms of infection.

*Read to the Section of Medicine at the Annual Meeting of the British Medical Association, Birmingham, 1958.

The relative importance of oropharyngeal virus and faecal virus in the transmission of the disease has not yet been established. It is my own belief that faecal–oral transmission is perhaps the commonest method of spread from child to child and to other members of the family. The important factor in the spread of virus is close personal contact.

As I have said, there appear to be "hot" families who are good disseminators and "cold" families who are poor disseminators of virus, and it appears that the spread of the virus in a community may take place as shown in Fig. 2.

It may be thought somewhat academic to discuss the spread of a virus the effects of which are gradually disappearing as a result of vaccination. My reason for mentioning it is that this type of spread may occur in other infectious diseases in which there may also be good and poor disseminators of the infectious agent.

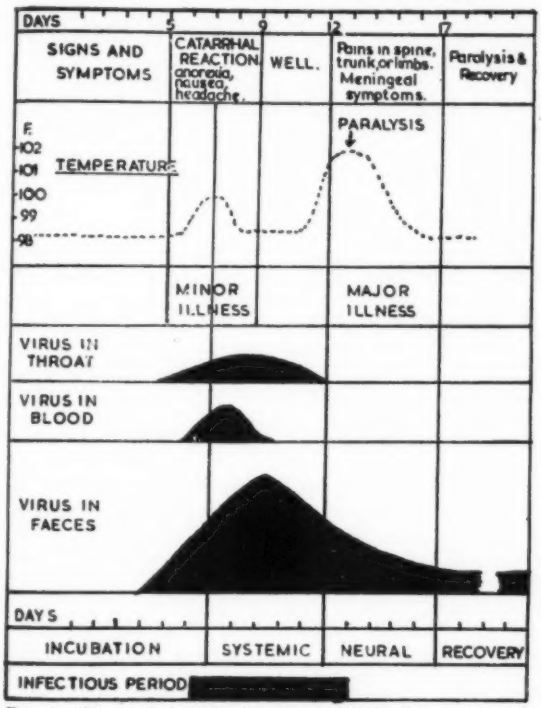

FIG. 1.—Time relationship between pathogenetic events and clinical picture in paralytic poliomyelitis.

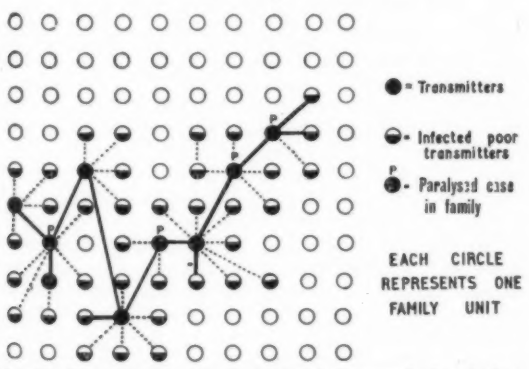

FIG. 2.—Diagrammatic representation of the spread of a virulent strain of poliomyelitis in a community.

Control of the Disease

This, then, brings us to the question of control. It is not possible to prevent the virus passing round the community. It may, however, sometimes be possible to avoid infection with a virulent strain by preventing contact of children with paralytic cases and their siblings.

Poliovirus is excreted in its largest amounts before the onset of paralysis, and the period of infectiousness is of relatively short duration (Fig. 1). If a child in a family is paralysed it is most probable that not only will the paralysed child be excreting a large quantity of virus but so also will the siblings. It therefore seems reasonable to quarantine the siblings for about one week—that is, during the period of expected high virus excretion. Unfortunately, in the majority of cases this will be closing the stable door too late.

So far as live virus vaccines are concerned I do not consider that any strains so far developed are satisfactory for wide-scale trials. In all studies which have been made with oral attenuated live virus vaccines it has been found that after feeding with these attenuated strains the virus multiplies in the gut and, like naturally occurring strains, is excreted in the faeces. Also like naturally occurring strains, these live vaccine viruses can spread from person to person. Furthermore, although the vaccine viruses which have been given by mouth are avirulent, they show an increase in virulence after multiplication in the gut of some people, and the excreted vaccine viruses cannot always be differentiated from the less virulent naturally occurring strains.

We have some evidence that naturally occurring strains passing through a community may alter in virulence. There is a wide variation in the virulence of polioviruses being excreted by healthy children, and while there is doubt about the stability of these naturally occurring strains there must also be doubt about the stability of excreted vaccine viruses which can spread from person to person.

May I say here that, although poliomyelitis has been more intensively studied than any other virus over the past ten years, we as yet have no idea why epidemics occur. Epidemics do not seem to be due to changes in the virus strains in the community. As Dr. Ritchie Russell has said, the paralytic case-fatality rate is now apparently uninfluenced by the nature of the epidemic. We have laboratory evidence which indicates that viruses recovered from paralysed individuals during a year of low incidence of the paralytic disease cannot be differentiated in the laboratory from epidemic strains.

Conclusion

We must conclude, then, that there is a host change which plays a large part in determining whether or not an epidemic will occur. It is not clear what this host factor is that permits a virus, which may be silently passing through a community and immunizing it one year, to produce an epidemic the next year. We have no idea why the virus should multiply better in some families than in others or why a particular child should become paralysed or even why poliomyelitis outbreaks are seasonal. If we only knew what the host factors were in determining whether the outcome of infection with a poliovirus was paralysis or a clinically unrecognizable immunizing infection we might be on the road to preventing the paralytic disease without using the formalinized Salk type of vaccine.

PRESENT SITUATION WITH FORMALIN-KILLED POLIOMYELITIS VACCINE*

BY

J. KNOWELDEN, M.D., D.P.H.

Lecturer, Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine

In recent years the attitude of the profession to prophylaxis has become far more sophisticated—it has been realized that if a prophylactic is introduced widely before its performance has been fully tested it may be exceptionally difficult to assess how well it works subsequently. Over fifty years ago, for example, the adoption of typhoid vaccination by the British Army without adequate evidence of protection provoked one of the most acrimonious correspondences ever to be conducted in the columns of the *British Medical Journal*, between Almroth Wright, the champion of the vaccine, and Karl Pearson, who pleaded for proper assessment of its effect. Precise information on the performance of this prophylactic in the field has waited on a study sponsored by W.H.O. in Yugoslavia only a few years ago (Cvjetanović, 1957). On the other hand, before the recently developed Salk vaccine was accepted for general use in North America in 1955, a controlled field trial had been carried out (Poliomyelitis Vaccine Evaluation Center, 1955).

North American Field Trial

The 1954 field trial of Salk vaccine was in two parts—in the first, the "observed control study," children in the second grade of school were vaccinated and their subsequent attack rates for poliomyelitis were compared with those of children in the first and third grades of the same schools. There are serious objections to this method of assessment. In the second part, the "placebo control study," volunteer children in the first, second, and third grades were allocated at random—just over 200,000 to receive Salk vaccine, and very nearly the same number to receive injections of a solution of similar appearance which should have had no influence on immunity to poliomyelitis. As the parents, children, and observers did not know which material an individual child had received the subsequent assessment provided an unbiased measure of the vaccine's performance.

In this placebo control study in the period May 1 to December 31, 1954, the paralytic attack rate in the vaccinated was 16 per 100,000, compared with 57 per 100,000 in the controls. The incidence in the vaccinated was only 28% of that in the unvaccinated, or, put another way, the vaccine was 72% effective against paralytic disease.

A small quantity of vaccine prepared in this country had been used in tests of antigenicity in adult volunteers. In view of the occurrence of cases of poliomyelitis in the U.S. associated with some commercial batches of vaccine released early in the summer of 1955, further use of formolized vaccine was abandoned for the time in Great Britain. Subsequently the Medical Research Council Committee on Safety Tests of Poliomyelitis Vaccine recommended that vaccine distributed in this country should not contain the virulent type 1 Mahoney strain used in the American vaccine and adopted up to that time elsewhere. By the winter of 1955–6 further batches of British vaccine were prepared containing the less virulent Brunenders strain as the type 1 component.

Medical Research Council's Trial

The Poliomyelitis Vaccine Committee of the Medical Research Council, reviewing the situation in consequence, considered that two questions needed answering urgently. (1) It was important to know first of all whether the substitution of the Brunenders strain for the Mahoney strain had reduced the capacity of the vaccine to protect against type 1 infection. (2) The American field trials had given evidence of protection in children 6–9 years of age only, with a slight suggestion of less protection in the youngest of this group. It was therefore also important to know whether formolized vaccine would protect younger pre-school children who have the highest rates of paralytic poliomyelitis in this country and are possibly subject to a different epidemiological background from that of American children. Consequently the Medical Research Council was invited to plan for an assessment of the protective effect of the vaccine which was to be issued in 1956 as part of the Health Departments' poliomyelitis vaccination programme in England, Wales, and Scotland.

It was impossible to set up a placebo control similar to that in the United States two years earlier. However, in the situation of shortage of vaccine, an assessment was made based on poliomyelitis occurring among about 150,000 children 1½–9½ years of age who received vaccine compared with that occurring among over 1,500,000 children of the same age who registered for vaccine but for whom none was then available (Medical Research Council, 1957b). The selection of whom to vaccinate from those registered was made according to month of birth—November for those born in 1947–50, roughly 5½–9½ years, and March and November for those born in 1951–4, roughly 1½ to 5½ years.

In the period July 1, 1956, to January 31, 1957, vaccinated children aged 5½–9½ years had only 16% of the paralytic poliomyelitis in registered unvaccinated children of the same age; for the younger group (1½–5½ years) the vaccinated had only 20% of the paralytic poliomyelitis in the unvaccinated. The apparent protection was 84% in the older group, 80% in the younger. I must emphasize here, *apparent* protection. Although the difference in rates achieved formal significance in both age groups, the number of cases was so small that no precise estimate of degree of protection could be made: in the younger group the true degree of protection could have been as little as 39%, and in the older only 6%. In the American trial, however, where the epidemics were more severe, the estimate of 72% protection was more precise, and at worst the true protection was unlikely to be less than 61%.

Information from Trials

In both American and British studies, therefore, significant protection against paralytic disease was shown. In both, however, the position with regard to non-paralytic disease was equivocal. For all so-called non-paralytic illnesses there was scarcely any difference in rates between vaccinated and unvaccinated in illnesses in either study. Dr. Galpine has rightly warned us of

*Read to the Section of Medicine at the Annual Meeting of the British Medical Association, Birmingham, 1958.

the unsatisfactory nature of a purely clinical diagnosis of non-paralytic poliomyelitis. If, then, we consider only aseptic meningitis in which there was laboratory confirmation by isolation of virus, both American and British studies show smaller attack rates for vaccinated than for unvaccinated children. However, the differences are nothing like as great as for paralytic illness and nowhere near approach significance. It looks, therefore, as if formolized vaccine may offer little protection against non-paralytic poliomyelitis. Furthermore, various studies in the United States show that Salk vaccine may produce little if any immunity to alimentary infection (Lipson, Robbins and Woods, 1956; Paul, Horstmann, Melnick, Niederman, and Deutsch, 1957; Fox, Gelfand, LeBlanc, and Rowan, 1958). Not only are vaccinated people as liable to infection as unvaccinated but the duration of excretion and the quantity of virus in the stools appear to be unmodified. Such vaccinated people are themselves as effective sources of infection to their associates as if they had never been vaccinated. In these respects artificially acquired immunity induced by killed virus vaccine differs from immunity derived from natural infection.

From this it follows that, however extensive our programme using killed-virus vaccine, we are unlikely to reduce the reservoir of poliovirus in the community. Even if formolized-virus vaccine produced lasting immunity to the paralytic complication of poliovirus infection, the programme would have to be maintained indefinitely, and to be successful would have to include a high proportion of those at risk. In this respect we should remember particularly the position of young adults going abroad—for example, in the armed Forces or Colonial Service—and the young parent with children of school age.

Number and Spacing of Injections

The 1954 field trials in North America used a course of three injections with an interval of one week between the first and second and of four weeks between the second and third injections. The British programme uses a two-injection course with an interval of three to four weeks. The antibody responses to such courses appear to be similar, and quite early the short interval between first and second injections was abandoned in North America, where the recommendation is now that, after the primary course of two injections at an interval of one month, a third injection should be given six or more months later. This recommendation finds support in the serological trials carried out by the M.R.C. Biological Standards Control Laboratory and their associates. These workers showed that in nearly all volunteer children who had no detectable antibody before inoculation the course of two doses produced an antibody response to all three types of virus (Medical Research Council, 1957a). After the second injection a decline in antibody levels occurred, especially marked for types 1 and 3. Nevertheless, a third injection 8 to 11 months after the primary course produced a booster response to all three types of virus to reach levels far higher than after the second injection (Medical Research Council, 1957c). Even when the interval between the second and third injections was extended to 18 months the same sort of booster response was seen (Medical Research Council, 1958).

The case for a third injection would seem clear on this evidence. Nevertheless we have no idea whether the booster antibody response to a third injection would be mirrored by additional protection against paralytic disease. There has been no rigid assessment of the degree of clinical protection since the three-injection course was adopted in North America, and in Britain the evidence is serological only because three injections have been given only to small experimental groups. Similarly, although antibody levels fall after vaccination we do not know whether there is a corresponding loss of protection. Both the British and the American assessment included a period of seven months only after vaccination. We have no direct evidence from the field, then, on which we can decide how long vaccination protects. We do not know what is the optimum antibody level we should try to maintain, or even whether there is such a fixed optimal level.

Conclusions

The facets of this problem on which we have sound information are those in which planned investigations have been made. We know from the field trials that formolized vaccine containing either Mahoney or the less virulent Brunenders type 1 component protects against paralytic disease, but probably does not prevent alimentary infection. We know that in Britain protection was afforded to both pre-school and primary-school-age children. We know from serological studies that older children and adults respond to vaccination in much the same way as younger children, but at the other end of the scale a recent paper gives evidence suggesting that the response of infants may be inadequate because of maternally transmitted antibody (Perkins, Yetts, and Gaisford, 1958). We know from the surveillance programmes in countries using killed-virus vaccines that no major catastrophe has occurred since the Cutter incident, although we cannot say categorically that no one has been infected with live virus.

On the other hand, we do not know how long the protection against paralytic disease lasts after primary vaccination with two doses. We do not know whether protection will be appreciably greater after a third injection or whether its duration will be prolonged. We do not know how best to use antibody responses in man to estimate his immunity to paralysis.

It may be impossible to set up the investigations which would fill these gaps in our knowledge. Certainly it must become more difficult to obtain this information the longer we use vaccine. We need this precise knowledge if we are going to formulate an intelligent vaccination programme. It would be a pity if we have to take important decisions in ignorance because we had not even tried to find out.

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ACTION OF "TESSALON" ON THE DYSPNOEA OF PATIENTS WITH CHRONIC LUNG DISEASE

BY

C. S. DARKE, M.D., M.R.C.P.

BERYL A. SNOWDEN, B.Sc.

Pulmonary Function Unit

D. VEREL, M.D., M.R.C.P.

J. J. DALY, M.B., M.R.C.P.

AND

W. R. LAYLAND, M.B., Ch.B.

Department of Medicine, University of Sheffield

From the Royal Hospital and City General Hospital, Sheffield

Michelson and Schiller (1957) investigated the effect of intravenously administered "tessalon"—a polyethylene glycol derivative of *p*-aminobenzoic acid—on the lung volume and ventilation in patients with obstructive pulmonary disease. They found that 2.5–10 mg. of tessalon produced symptomatic relief with an increase in both depth and volume of respiration in most instances and an increase in the minute-volume up to twofold. There was no significant change in lung volumes or expiratory flow rate. Their favourable report suggested that the drug should be tried in patients in whom chronic lung disease had produced a disabling grade of dyspnoea.

The investigation was divided into two parts: the acute effect of intravenous administration and the prolonged action of oral therapy using a double-blind clinical trial.

"Acute" Trial

Method

The effect of intravenous tessalon upon the minute-volume, intrathoracic pressure, air flow, and respiratory rate, pulse rate, and blood pressure was measured. All the subjects were volunteers. The nature of the experiment was explained to them, but no indication of the possible effects of the drug was given apart from the statement that it had been recommended for use in patients with chest disease.

The subject sat in a comfortable chair, connected by a soft rubber mouthpiece to a Lilly pneumotachograph. This was connected to a respiratory anemometer which was designed to read air outflow in litres. A "polythene" tube attached to a thin rubber balloon was passed through one nostril into the lower third of the oesophagus and was held in place by a nose-clip, which also prevented any air flow through the nose. Changes in intrathoracic pressure and rate of air flow through the pneumotachograph were continually recorded on a Cambridge multi-channel recorder. Normal saline was slowly infused through an intravenous needle attached to a blood-transfusion giving set introduced into a vein in the right arm. Around the left arm was placed a sphygmomanometer cuff, and blood pressure was recorded using the criteria of the Cardiac Society (1939).

The volume of air expired was recorded at half-minute intervals throughout the investigation. When steady readings were being obtained, the tracings of the flow rate and pressure were started. Tessalon was injected into the rubber tubing of the giving set and washed into the circulation by increasing the rate of the saline transfusion. No indication was given to the subject that the administration was taking place. At intervals before and after injecting tessalon, measurements of the pulse rate and blood pressure were recorded and all readings and tracings were continued until five minutes after the last dose was given.

Tessalon, 5 or 10 mg., was administered at intervals of two to five minutes. The total amounts ranged from 5 to 20 mg. (Table I). After the final injection the patient was asked if he had noticed any symptoms.

Results

Observations were made on four normal people and seven patients with chronic lung disease.

Minute-volume, respiratory rate, pulse rate, blood pressure, air flow, and intrathoracic pressure showed no significant change during periods of up to 21 minutes from the initial injection of tessalon in patients at rest or exercising on a bicycle ergometer (Table I). One patient (No. 10) suffering from spasmodic asthma said that her breathing felt easier at the end of the investigation and her desire to cough had disappeared. The only adverse effect was a severe headache lasting 12 hours reported by a patient with diffuse interstitial pulmonary fibrosis (No. 9). The effect of increasing the dosage to a maximum value of 45 mg. was tested on another patient not included in the above investigation. The respiratory rate, blood pressure, and pulse rate did not change, and the patient experienced no symptoms.

TABLE I.—*Effect of Intravenous Injection of Tessalon in 11 Subjects. Statistical Analysis Shows that the Minute-volume after Injection did not Differ Significantly from that before Injection ($P=0.5$)*

No.	Sex and Age	Diagnosis	Dose (mg.) and Divided Doses of Tessalon	Mean Readings Three Minutes Before First Injection				Mean Readings Following Intravenous Tessalon			Mean Reading of Minute-volume (l./min.) During Three-minute Intervals Following Tessalon						
				B.P.	P.R.	R.R.	l./min. M.V.	B.P.	P.R.	R.R.	1–3	4–6	7–9	10–12	13–15	16–18	19–21
1	M 28	Normal	5	160/95	80	22·1	17·8	150/95	78	21·4	18·4	16·6	16·5	16·4			
2	M 25	"	10	170/80	120	21	18·2	170/80	120	23	16·5	17·2	16·7	17·0			
3	M 38	"	15 (5, 5, 5)	140/90	76	17·5	15·5	140/95	84	17·8	17·3	16·1	17·6	14·9			
4	M 51	Chronic bronchitis and emphysema	10	140/90	96	16	14·3	145/95	94	16	13·3	14·3	13·8				
5	M 37	Cor pulmonale ..	10	125/80	120	20	15·1	120/80	120	21	16·8	17·4					
6	M 22	Normal	10		100	19·5	19·9		100	19·2	21·9	20·4	23·0				
7	M 54	Chronic bronchitis and emphysema	15 (5, 5, 5)	150/80	96	15	16·4	160/80	92	16·6	18·1	18·1	21·0	18·3	18·4	22·6	
8	M 58	" "	15 (5, 5, 5)	220/110	120	26	25·4	195/90	128	27·4	27·8	26·3	26·6	27·0			
9	M 56	Interstitial pulmonary fibrosis	15 (10, 5)	150/80	76	15	17·8	150/90	74	16·8	18·6	18·6	18·3	22·1			
10	F 29	Spasmodic asthma	20 (5, 5, 5, 5)	120/70	100	22	15·0	120/70	100	22	16·6	17·7	16·0	14·0	15·2	18·2	17·2
11	F 51	Chronic bronchitis and emphysema	20 (10, 5, 5)	120/80	88	21	13·9	125/70	86	22·6	16·9	16·2	16·7	16·6	16·8	18·9	

Maximum Breathing Capacity.—Two further patients suffering from diffuse interstitial pulmonary fibrosis were given a control injection intravenously followed five minutes later by an injection of 5 mg. of tessalon. The maximum breathing capacity and respiratory rates were measured at intervals of one, three, and five minutes after each injection, using a spirometer. No significant change was found after tessalon was injected.

Clinical Trial

The tessalon used in this trial was prepared in 100-mg. capsules. Identical placebo capsules were also supplied by the manufacturers. Each patient acted as his own control. Either the placebo or tessalon capsules were given for one week in a random order, and the allocation was the responsibility of the hospital pharmacist. At no time during the investigation were the medical staff told whether the patient was receiving tessalon or the placebo. At the end of the trial every patient had had one week on tessalon and one week on the control capsules.

Two groups of out-patients were investigated. Tessalon, 100 mg. t.d.s., was tried on 20 patients (14 male, 6 female) who were dyspnoeic on effort as a result of chronic lung disease. At the beginning of the trial each subject was examined and the respiratory system was assessed clinically. The forced vital capacity and the volume expired in the first 0.75 second were measured, using a Gaensler spirometer: the expired volume of air in three consecutive minutes was determined with a respiratory anemometer and the respiratory rate was counted. A week's supply of capsules, in addition to any treatment he might already be receiving, was given to the patient. The following week the clinical examination and respiratory function tests were repeated and a further supply of capsules was dispensed. A final examination, and measurements, were made at the end of the fortnight. All the clinical examinations were made by the same observer.

In six further patients (four male, two female) suffering from diffuse interstitial pulmonary fibrosis the effect of the therapy on the ability to exercise was observed by stepping 20 times on and off a 9-in. (23-cm.) step. Each patient was asked to report any change in symptoms.

Results

Of the 26 patients in the trial, 3 were excluded from the analysis. Of these, a man with chronic bronchitis and emphysema stopped taking the capsules after four days because of increasing dyspnoea and cough. The capsules were the placebo. A second man was admitted to hospital on the 13th day with an exacerbation of his chronic bronchitis, and a third patient, a female, had to be admitted to the ward at the final examination with a functional laryngeal stridor, so that it was impossible to complete the respiratory function studies.

Of the 23 patients finally included in the trial, 14 were given tessalon in the first week and placebo capsules during the second week: the remaining nine received the capsules in the reverse order.

Respiratory Function Tests.—Although slight changes in the values of the minute-volume, respiratory rate, forced vital capacity, and timed vital capacity (0.75 second) were observed following a course of tessalon, similar changes were produced by the placebo, and none of them was statistically significant (P varying from 0.5 to 0.8).

The exercise tolerance was not affected in the six patients in whom it was measured.

Clinical Assessment.—Table II shows the clinical state in 16 subjects examined at all three attendances. No change was observed in eight of the patients throughout the trial. In six the administration of tessalon was followed by a reduction in adventitious sounds (Nos. 2, 3, 5, 10, 12, and 14). In two patients an increase in adventitious sounds was observed after a week on tessalon therapy (Nos. 7 and 16). These numbers are not large enough for valid statistical analysis.

TABLE II.—*Effect of Oral Tessalon and Placebo on the Clinical Signs in the Lungs in 16 Patients with Chronic Lung Disease*

No.	Sex	1st Attendance	2nd Attendance	3rd Attendance
			After Tessalon	After Placebo
2	M	Forced expiratory rhonchi	Chest clear	Chest clear
5	F	Generalized rhonchi	,, ,,	Generalized rhonchi
6	F	,,	Generalized rhonchi	,,
7	F	Chest clear	High-pitched sibili	Chest clear
10	M	High-pitched sibili	Chest clear	High-pitched sibili
11	M	Expiratory rhonchi	Expiratory rhonchi	Expiratory rhonchi
12	M	,,	Chest clear	Generalized rhonchi
16	M	Chest clear	Expiratory rhonchi	Forced expiratory sibili
18	F	Forced expiratory sibili	Forced expiratory sibili	,, ,,
19	M	Chest clear	Chest clear	Chest clear
			After Placebo	After Tessalon
3	M	Generalized rhonchi	Generalized rhonchi	High-pitched sibili
4	F	,,	,,	Generalized rhonchi
8	M	Chest clear	Chest clear	Chest clear
13	M	Generalized rhonchi	Generalized rhonchi	Generalized rhonchi
14	M	Scattered rhonchi	Scattered rhonchi	Forced expiratory rhonchi
15	M	Generalized rhonchi	Generalized rhonchi	Generalized rhonchi

Subjective Changes.—All 23 patients in the trial were asked at the second and third visits if they had noticed any changes in their symptoms and had had any adverse effects from the capsules. Improvement in symptoms was reported by seven. A gradual lessening in symptoms throughout the trial was noticed by three of these, without any apparent relation to the tessalon. The remaining four all stated there was some improvement at one visit but not at the other. Two were found to have had relief from tessalon and two from the placebo. The chest condition was unchanged at both attendances in 16 patients. Six of these complained of adverse effects, three developed headaches while on tessalon, and three developed symptoms while taking the placebo. At one attendance two patients reported an increased feeling of well-being. They had both had a week of placebo capsules.

Discussion

Animal experiments have shown that tessalon will selectively depress the peripheral nerve endings in the lung concerned with the regulation of normal respiration (Bein and Bucher, 1957). The observations of Michelson and Schiller (1957), however, suggested that the symptomatic relief obtained in asthmatic patients did not depend on this mechanism. They reported that tessalon induced a sensation of ease of breathing with increased minute-ventilation. We have found no change in either symptoms or objective measurements of lung function in patients with chronic lung disease after intravenous tessalon, or after oral treatment for a week. In the double-blind trial both adverse and favourable symptoms were reported equally with the placebo and the drug, but headache was noted only in patients taking

tessalon. A severe headache also occurred in a patient given intravenous therapy. Naegeli (1956) has also found this symptom in patients treated with tessalon.

We are unable to confirm the antitussive action of tessalon that has been reported (Giuliano and Rossa, 1955; Bucher, 1956, Herzog, 1956; Naegeli, 1956; Neumann, 1956; Simon, 1957; Shane *et al.*, 1957). One patient noticed considerable relief from coughing while taking both the placebo and the drug, and another lost the desire to cough after intravenous administration of tessalon. All our patients, however, had a severe grade of dyspnoea with a relatively minor degree of cough.

Summary

Tessalon—a polyethylene glycol derivative of *p*-aminobenzoic acid—has been given intravenously in doses up to 45 mg. without causing symptoms or having any measurable effect on minute-volume, air flow, intrathoracic pressure, maximum breathing capacity, respiratory rate, pulse rate, and blood pressure in four normal subjects and 10 patients with chronic lung disease.

A double-blind trial of tessalon in 23 patients with chronic pulmonary disease did not have any beneficial effect.

We thank Dr. T. Hanley, of Ciba Laboratories Ltd., for supplying the preparation of tessalon; Professor C. H. Stuart-Harris for permission to use patients under his care at the Royal Hospital, Sheffield; Messrs. J. E. Cocking and J. Earnshaw, the chief hospital pharmacists, for their co-operation in organizing the double-blind trial; Mr. D. S. Kerridge for his statistical advice; Mr. D. E. Woolhouse for his technical assistance; and Miss M. P. Middlebrook for her secretarial assistance.

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DOUBLE CARDIAC ARREST WITH SURVIVAL

BY

BASIL L. FINER, M.B., F.F.A. R.C.S., D.A.

AND

BENGT O. NYLÉN, Med. Lic.

From the Departments of Anaesthesia and Plastic Surgery, University Hospital, Uppsala, Sweden

During tracheobronchial manipulations cardiac arrest is a well-known complication. Such arrest may occur at separate operations on the same patient (Lampson, 1951), repeatedly at one operation (Knowles, 1953), or during angiocardiography (Holmdahl and Gyllenswärd, 1954). If during a non-urgent operation arrest occurs, it is probably safer to terminate the operation as soon as possible after the heart is restarted. However, if the operation is urgent, the possibility of further cardiac impairment during or following a necessary operation, once the heart has been restarted, must be weighed against the functional impairment resulting if the operation is not completed. This problem is illustrated by the following case report.

Case Report

A man aged 24 years was involved in a factory explosion and suffered 10% third-degree burns of both hands, face, and left thigh.

On three occasions (March 12, 14, and 20, 1957) he was anaesthetized and orally intubated under "narkotal" (an ultra-short-acting barbiturate), suxamethonium, pethidine, nitrous oxide, and oxygen, for cleaning and dressing of the burns, without untoward results.

March 21.—He was anaesthetized by one of us (B. L. F.) for the first time. It was noticed that he suffered very great pain in his hands and was in a state of extreme anxiety, in spite of premedication with morphine, 10 mg., and scopolamine, 0.3 mg. While a vein was being found for intravenous injection, he was moaning, restless, and terrified of the repeated attempts at venepuncture. Owing to the rather extensive third-degree burn surface in this case no cut down of the vein had been made. Anaesthesia was induced with narkotal, 300 mg., and suxamethonium, 100 mg. A No. 10 Magill cuffed tube was inserted orally and connected to the anaesthetic machine, the patient being ventilated with nitrous oxide and oxygen. At this stage he rapidly turned white and the pupils became widely dilated. Spontaneous respiration had not returned after the suxamethonium. His pulse could not be felt and cardiac sounds were not heard. 100% oxygen was administered, and within two minutes of detection of cardiac arrest one of us (B. O. N.) made a left submammary intercostal incision, without bleeding from the skin vessels, and a hand was placed around the pericardium. Immediately before massage, spontaneous heart beats returned, the skin wound began spurting, the colour became pink, and the pupil returned to normal size. Blood pressure and pulse became stabilized at 110 and 80 respectively. The operation was postponed to allow the patient to awaken, which he did on extubation. Apart from even greater anxiety after being told the reason for his submammary wound, cerebral function seemed normal.

March 26.—A further excision of granulation tissue of the burnt hands was performed. Premedication was with promethazine, 50 mg., pethidine, 100 mg., and atropine, 0.5 mg. The patient was still very frightened. Induction was with nitrous oxide and oxygen, venepuncture being avoided until he was asleep. Narkotal, 300 mg., pethidine, 50 mg., and suxamethonium, 200 mg., in intermittent doses were administered, but without intubation, and the operation proceeded without incident. During the operation an infusion was set up in the foot and continued until the following day. In this way a venepuncture was not necessary while the patient was awake, and the cause for some of his fears would be removed.

March 27.—Because of the second/third-degree burns in his face and also because of his state of anxiety it was thought that the best anaesthesia would be by intubation. He was premedicated with chlorpromazine, 25 mg., morphine, 10 mg., and scopolamine, 0.3 mg. Induction was by chlorpromazine, 10 mg., pethidine, 50 mg., narkotal, 300 mg., suxamethonium, 50 mg., and local analgesic spray to the larynx and trachea. A No. 10 Magill cuffed tube was passed and maintenance was with nitrous oxide and oxygen. At this stage the pulse was 80 and blood pressure 110, the skin colour was pink, and the pupils were of normal size. Very rapidly over the next minute the pulse became increasingly faster until it was uncountable and then impalpable, the blood pressure dropped to zero, the skin became pale, and the pupils became widely dilated. No heart sounds were heard and the previous submammary incision was reopened. The heart was in asystole and cardiac massage was applied. After about 10 compressions

of the heart, spontaneous beating recommenced, while blood pressure, pulse, skin colour, and pupils returned to normal. It was then discussed whether or not operation should continue, and it was decided to proceed with the skin grafts. For adequate working function of the patient's hands and a good result for the face they must be grafted as soon as possible, as in a subsequent anaesthesia he might develop an irreversible cardiac arrest. The operation lasted two hours (including cardiac arrest) without further incident, and the patient awoke immediately after extubation. He made an uneventful recovery except for a transient pleural effusion, which was tapped under local analgesia without further recurrence. Electrocardiograms taken on March 23, 27, 28, and 30 were normal.

The patient left hospital two weeks after the grafting. When seen three months later his hand function was fair, though he was still very anxious. Otherwise cerebral function was good. Later, operations were carried out seven times on the hands and face under local analgesia. On the hands the method used was brachial plexus block. There has been no further incident in connexion with these anaesthesias. When the patient was seen again one year and three months later, his anxiety was much less and the electrocardiogram continued to be normal.

Discussion

That cardiac arrest followed the fourth and sixth anaesthesias with intubation, but not the fifth without intubation, suggests that intubation triggered off cardiac arrest. Why this had not occurred after any of the first three intubations is not clear, but the patient's increasing fear may have passed a critical point at the fourth anaesthesia. The resulting increased reflex excitability, together with the viscero-cardiac reflex (Keating, 1956) from intubation, might then have been enough to stimulate cardiac arrest. It seems clear that the possibility of cardiac arrest on intubation should be kept in mind if a patient comes to operation in great fear and/or pain. If it is possible to avoid intubation, other methods of anaesthesia should be employed. However, if (*a*) cardiac arrest has occurred, (*b*) the patient is young and otherwise healthy, and (*c*) cardiac resuscitation is successful with circulation restarted within the safety time-limit (less than three minutes without anoxia preceding the cardiac arrest) it is recommended that the operation be continued.

Summary

A case report is presented of a patient, in great pain and anxiety, who on two occasions developed cardiac arrest immediately after intubation.

On the first occasion, following successful cardiac resuscitation, the operation was postponed, but after the second successful resuscitation, operation being urgent and the patient young and otherwise fit, it was completed without further incident.

It is suggested that cardiac arrest under anaesthesia for an urgent operation, in a young and otherwise fit patient, need not warrant postponement of the operation if the heart can be successfully restarted.

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HEINZ-BODY ANAEMIA DUE TO DAPSONE

BY

R. S. SMITH, M.A., M.B., B.Chir.

Graduate Assistant in Pathology, University of Oxford

AND

SUZANNE ALEXANDER, M.B., B.S.

Registrar in Dermatology, Radcliffe Infirmary, Oxford

Dapsone (diaminodiphenyl sulphone), originally introduced for the treatment of leprosy, has since 1953 (Kruizinga and Hamminga, 1953) been used in the treatment of dermatitis herpetiformis. Many authors have found it of great value (Vickers, 1954; Morgan *et al.*, 1955; Alexander, 1955), and it is preferred by many doctors and their patients to sulphapyridine, liquor arsenicalis, etc., which had previously been used to suppress the symptoms of this condition.

In dermatitis herpetiformis the minimum dose of dapsone required to suppress the symptoms varies greatly in different patients, some requiring as much as 200 mg. daily, while others are controlled by 50 mg. daily or less. Side-effects during dapsone therapy are common. The manufacturers give warning of the dangers of haemolysis; other side-effects which have been reported are liver damage, drug rashes, depression, which can be very severe, and, recently, agranulocytosis (McKenna and Chalmers, 1958).

It is well recognized that anaemia, sometimes severe, can occur during the course of dapsone therapy (Allday and Barnes, 1951; Kruizinga and Hamminga, 1953; Morgan *et al.*, 1955; Alexander, 1955). Early recognition of the onset of this state is important, and the detection of Heinz bodies is a most useful test. These are small refractile granules found in the red blood cells in many cases of drug haemolytic anaemia. They cannot usually be seen in a routinely stained blood film, but they are readily demonstrated by a simple technique, using a supravital stain.

Numerous Heinz bodies were found in a patient (Case 1) who developed haemolytic anaemia while taking dapsone, and as a result of this finding we performed the test in other patients.

Technical Methods

Demonstration of Heinz Bodies.—Method I:—A few drops of blood are mixed with about double their volume of 0.5% methyl violet in isotonic saline (this solution must be filtered before use). After standing for a few minutes, a drop is examined under a coverslip with the oil-immersion objective. *Method II* (permanent preparations):—A few drops of blood are mixed with about twice their volume of isotonic saline. The tube is centrifuged until the cells are deposited and the supernatant fluid is poured off. The cells are resuspended in a solution of 0.5% methyl violet in isotonic saline (filtered immediately before use). The tube is centrifuged again and films are made at once from the deposit; these are air dried and mounted without any fixation or counterstain.

Blood may be taken by finger prick or by venepuncture into citrate or ethylenediamine tetra-acetate (E.D.T.A.). By either of the above methods Heinz bodies are shown as darkly stained discrete

particles. The red cells are pale yellow, almost colourless; reticulocytes show a diffuse mauve mottling.

Other Methods.—All other haematological techniques used were those recommended by Dacie (1956).

Case 1

A 76-year-old farmer had been well until August, 1956, when he first noticed a blister on his left thigh. He attributed this to a hot-water bottle burn, although he could not remember having burned himself. Healing was very slow. From that time onwards he developed many more small blisters; they appeared on normal-looking skin, were extremely itchy, and on bursting left indolent ulcers. He was admitted to hospital on March 27, 1957, when he was found to have widespread dermatitis herpetiformis. He was hypertensive (blood pressure 210/110 mm. Hg). In spite of local treatment combined with bed rest, his condition became worse.

Twelve days after admission he was given dapsone 50 mg. daily; after three days this was increased to 100 mg. twice daily. Three days later, on April 14, no new blisters were developing, and the dapsone seemed to control his dermatitis herpetiformis adequately. However, on April 26 he went into cardiac failure but responded well to treatment with digoxin, aminophylline, and mersalyl. Dapsone was continued, and subsequently he developed a haemolytic anaemia. By June 4 he was cyanosed; his haemoglobin had fallen to 72% (10.7 g./100 ml.), and Heinz bodies were found in 50% of his red blood cells. A blood film showed numerous fragmented red cells, and the reticulocyte level was 10%. The white-cell count was 17,800/c.mm.; a small quantity of methaemoglobin was detected in the red cells; the red-cell osmotic fragility was normal. Dapsone was at first reduced in dosage, then withdrawn. The Heinz bodies gradually disappeared and fragmented cells were no longer seen in the blood films. Fig. 1 summarizes the findings in the blood during this period; Fig. 2 is a photograph of the blood on June 4, stained to demonstrate the Heinz bodies.

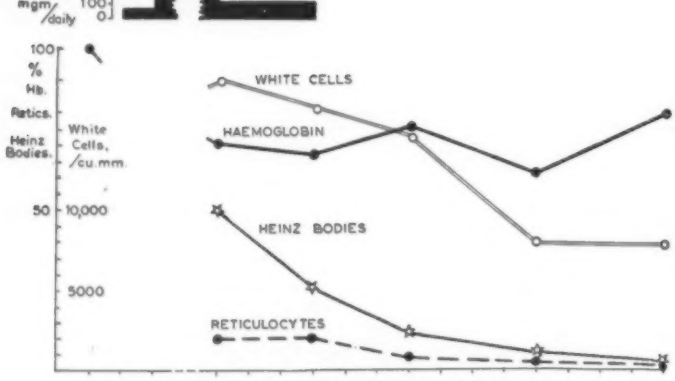

FIG. 1.—Course and treatment in Case 1.

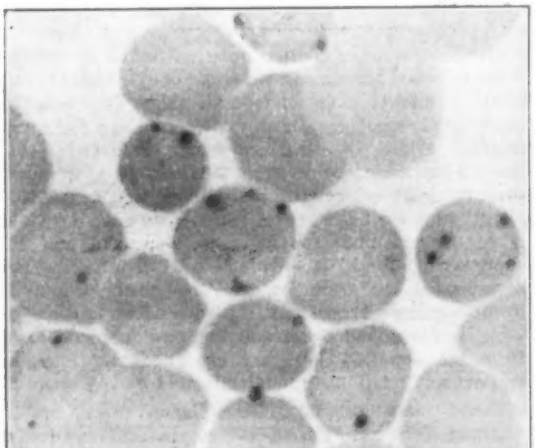

FIG. 2.—Heinz bodies in the blood in Case 1.

Case 2

A married woman aged 52 first developed dermatitis herpetiformis in 1932. She had not noticed any relief from her itching until 1955, when she began treatment with sulphapyridine (0.5 g. twice daily). By 1957 the dermatitis herpetiformis was well controlled. Her blood picture at this time was normal; on May 13 her haemoglobin was 92% (13.6 g./100 ml.) and white cells 7,800/c.mm. As she felt very depressed, on June 24 the sulphapyridine was replaced by dapsone 100 mg. twice daily. On July 22 a blood count showed a haemoglobin level of 72% (10.7 g./100 ml.), the white-cell count was 9,300/c.mm., and some fragmented cells were seen in a blood film.

Unfortunately the test for Heinz bodies was not carried out on July 22; the patient was seen again 48 hours later for this purpose, when Heinz bodies were found in 40% of her red blood cells, and a reticulocyte count was 8%. Dapsone was discontinued and sulphapyridine (0.5 g. twice daily) restarted. Her dermatitis herpetiformis has been well controlled on this dose.

Case 3

A married man aged 56 was quite well until 1953, when he developed dermatitis herpetiformis. He began treatment with sulphapyridine 0.5 g. twice daily in 1954, but had to stop this after three months because of malaise and headaches. In 1955 treatment with dapsone was instituted, beginning with a dose of 100 mg. daily and later increased to 100 mg. twice daily. His itching became well controlled after two months, and he was gradually able to reduce the dose to about 100 mg. every third day.

In July, 1957, he was noted to have blue lips, and a routine blood count showed a haemoglobin of 93% (13.8 g./100 ml.), the white-cell count was 7,000/c.mm., and Heinz bodies were present in 14% of his red blood cells. Dapsone was still further reduced, and in November his haemoglobin was 96% (14.1 g./100 ml.) and reticulocytes 1.5%; Heinz bodies were present in 14% of his red blood cells. He then remained well, taking 100 mg. of dapsone once a week, until July, 1958, when he developed erythema multiforme and pneumonia, and had to be admitted to hospital. His dapsone was increased to 100 mg. daily; five days after admission his haemoglobin was 70% (10.4 g./100 ml.), and Heinz bodies were present in 25% of his red cells. Dapsone was reduced and four days later his haemoglobin was 83% (12.3 g./100 ml.), and Heinz bodies were present in 26% of the red blood cells. The reticulocyte level was 4.2%, white-cell count 5,200/c.mm., and blood plasma bilirubin 0.3 mg./100 ml. Two days later he had a cerebrovascular accident; he made a complete and uneventful recovery from this, as well as from his pneumonia and erythema multiforme. At the time of writing he was well apart from hypertension—blood pressure 220/120.

Case 4

This patient, a man of 52, was found to have dermatitis herpetiformis in September, 1956. He was treated by

dapsone, 50 mg. twice daily, which completely controlled his itching and prevented further blister formation. Frequent blood counts showed no anaemia. However, on July 11, 1957, Heinz bodies were found in 8% of his red cells. His haemoglobin at that time was 84% (12.4 g./100 ml.) and his white-cell count 6,100/c.mm. He continued on the same dose of dapsone and remained free from symptoms.

Discussion

The formation of Heinz bodies in the peripheral blood usually indicates chemical poisoning. Fertman and Fertman (1955) list numerous substances which have been shown to cause the formation of Heinz bodies. These include aniline and its derivatives, and nitro-compounds of benzene and toluene; many of these substances are used in industry, and some, particularly the sulphonamides, are of considerable medical importance.

The chemical nature of Heinz bodies, and the mechanism by which they are formed, are not well understood. It is generally agreed that they indicate haemoglobin degradation, and possibly damage to the red-cell stroma in addition. The affected cells have a reduced life-span, and a haemolytic anaemia will develop if the affected cells are eliminated more rapidly than they can be replaced. In this case the Heinz bodies are more numerous, fragmented red cells may be seen in blood films, and the haemoglobin value falls. The anaemia is, in many cases, aggravated by the formation of methaemoglobin or other abnormal pigments.

Moeschlin (1940), in describing the effects of sulphonamides on the red blood cells, thought that if the number of red cells containing Heinz bodies rose above 20% a haemolytic anaemia might develop and the patient should be watched closely. Heinz body levels of over 50% were associated with a frank haemolytic anaemia. The findings in our cases, where the Heinz bodies developed during dapsone therapy, were similar. Thus in Cases 1, 2, and 3 Heinz bodies were numerous, reaching levels of 50%, 40% and 26% respectively. In these cases the haemoglobin had fallen, fragmented cells could be seen in blood films, and reticulocytes were fairly numerous. These findings suggested that a haemolytic anaemia was developing. Case 4 showed small numbers of Heinz bodies (8%) and the drug was continued without the development of anaemia.

It seems that if there are only a small number of Heinz bodies present the haemoglobin will be maintained at a satisfactory level, even if dapsone is continued. If Heinz bodies become more numerous and it is essential to continue treatment a reduction in dosage may be enough to prevent the development of a haemolytic episode. We believe that examination of the blood for Heinz bodies is a valuable procedure in the control of dapsone therapy. It is a simple and rapid test, requiring no special equipment, and can be performed equally well on capillary or venous blood.

Summary

Four cases are described in which blood showed the formation of Heinz bodies following the administration of dapsone.

Three of these patients, whose blood showed numerous Heinz bodies, developed haemolytic anaemia.

Examination for Heinz bodies is a simple and useful test in the control of patients receiving dapsone.

We thank Dr. H. R. Vickers for his help and encouragement. We are indebted to Dr. A. H. T. Robb-Smith and Dr. R. G. Macfarlane for helpful criticism and advice.

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NYDRANE AS AN ANTICONVULSANT

BY

N. KAYE, M.B., B.S.

I. H. JONES, M.B., B.S.

AND

G. K. WARRIER, M.B., B.Sc., M.R.C.P.Ed.

From the Neurological Departments of the General Infirmary at Leeds and Pinderfields Hospital, Wakefield

During recent years several papers have appeared commenting on the use of "nydrane" as an anticonvulsant drug (Gotten, Hawkes, and Tyrer, 1951; Hawkes, 1952; Merlis and Martin, 1956; Hoenig, Crotty, and Chisholm-Batten, 1956; Robinson, 1957; Sharpe, Dutton, and Mirrey, 1958; and others). Beneficial effects on the convulsive and mental states have been claimed, together with remarkably low toxicity. In the course of routine work in the neurological departments of the General Infirmary at Leeds and Pinderfields Hospital, Wakefield, this drug has been tried in the treatment of epileptics, both in-patient and out-patient. Our results have differed in some respects from those of other workers, and we have thought it worth while reporting our experiences.

The chemical and pharmacological characteristics of nydrane have been widely reported. It differs from all other anticonvulsants in being a benzylamide, and its chemical composition is N-benzyl-β-chlorpropionamide. It is found experimentally to protect against artificial convulsions in animals. Its effect is said to be maximal in two hours and to last up to five hours (Harned *et al.*, 1953). It is supplied in 0.5-g. tablets.

Material

Up to the time of writing, 27 patients under the care of Dr. Hugh Garland have been treated with nydrane, either alone or in combination with other drugs. These patients comprise the present series, which is unselected. There were 14 males and 13 females. Their ages ranged from 11 to 55 years. The duration of attacks varied from 2 to 50 years. In general it was poor response to other drugs (barbiturates, hydantoinates, and primidone), in combination and in high dosage, which led to the trial of nydrane. Most of these patients responded to some extent to former treatment but continued to have attacks with a frequency of from once monthly to several a day; most were having several weekly. The low toxicity claimed for nydrane led us to try it in two patients with less frequent attacks requiring very high dosage of primidone and phenytoin

TABLE I.—*Types of Attack*

	No. of Patients
Major epilepsy	22
Focal ,,	3
Psychomotor and other temporal lobe variants	12
Minor absences	1
More than one type	10

sodium. The types of seizure are given in Table I. All had unequivocal attacks of epilepsy and all, except five, had electroencephalographic evidence of epilepsy; 13 had personality disorders.

Methods

It was usual to add one 0.5-g. tablet twice or thrice daily to the previous medication as a first step, with the aim of controlling the attacks. In 17 patients one of the previous drugs was then diminished and the nydrane dosage increased slowly up to a maximum of eight times daily (4 g.), depending upon the response. The more severe cases were admitted to the neurological wards at Pinderfields Hospital for this changeover because of the theoretical danger of status epilepticus. In the remaining 10 patients nydrane was added without reduction of other drugs and was continued for periods varying from three months to one year.

The difficulties in assessing the effects of treatment of epilepsy are notable, and most prominent among them are: (1) obtaining accurate evidence of the frequency of fits; (2) ensuring that all the prescribed treatment is taken regularly; and (3) assessing the "suggestive effect" of a tablet new to the patient.

An attempt was made to correct for these factors so far as was possible in those patients admitted to hospital in the following ways: (1) each patient was asked to note every fit on a single sheet of paper—these records were checked against our own observations and evidence from such witnesses as the nursing staff and other patients in the ward; (2) the taking of tablets could be supervised; and (3) in six patients inert dummy tablets were interchanged with the active tablets at intervals of not less than one week, without the patient's knowledge. One of us (G. K. W.) worked full-time in the wards and observed these patients continually.

Results

In assessing the response we adopted the method used by Hawkes (1952). Three categories of severity are defined, as judged from the frequency of attacks: excellent, "patients were seizure-free or had only occasional attacks"; good, patients were having one to four attacks a month; and bad, patients were having one or more attacks weekly. The appropriate category is determined for each patient from the average frequency of attacks (*a*) during the year preceding treatment with nydrane, and (*b*) whilst on treatment with nydrane. The distribution is shown in Table II.

Table III shows the placing of each patient before and after treatment with nydrane. It will be seen that three patients improved, six became worse, and 18 remained unchanged. In Case 25 the minor absences were controlled by troxidone completely before nydrane was started. In Case 4 the attacks increased to such an alarming extent that it was felt that the patient might go into status epilepticus if her former treatment was not reinstated.

Change in severity of the attacks was not a noticeable feature. No particular effect on the mental state was noted, apart from that directly attributable to the reduction in the frequency of seizures, when this occurred.

TABLE II

	Before Nydrane	With Nydrane
Excellent	2	3
Good	13	9
Bad	12	15
Total	27	27

TABLE III

Case No.	Type of Attack	Before Nydrane	After Nydrane
	Nydrane Substituted		
1	Temporal lobe	B	G→B
2	Focal sensory. Major	E	G
3	Temporal lobe. ,,	G	E→B
4	Major	B	B (status)
5	,,	B	B
6	Temporal lobe	B	B
7	Temporal lobe. Major	G	G
8	Major	G	G
9	Temporal lobe	B	B
10	Temporal lobe. Major	B	B
11	Major	G	G
12	Temporal lobe. Major	B	B
13	,, ,, ,,	B	B
14	,, ,, ,,	G	B
15	Major	B	G
16	,,	G	B
17	Focal motor. Major	G	B
	Nydrane Added		
18	Major	G	B
19	Focal motor	G	G
20	Temporal lobe	B	B
21	Major	B	B
22	,,	G	G
23	,,	G	G
24	,,	E	E
25	Major. Minor absences	B	E
26	Temporal lobe. Major	G	E
27	,, ,, ,,	G	G

E=Excellent. G=Good. B=Bad.

In three patients treated in hospital all other drugs were replaced by nydrane in presumably comparable dosage, but the number of fits increased. Other drugs were then added to control the attacks to a tolerable level. The nydrane was then replaced by inert dummy tablets and thereafter the true and inert tablets were interchanged at intervals. During this interchange the clinical state remained unaltered.

In three further in-patients nydrane was added and the other drugs were reduced in dosage. The number of fits increased. Nydrane was then replaced by dummy tablets and no further increase resulted. The original medication was reinstated and the number of fits decreased.

Side-effects.—Within 48 hours of starting nydrane, two patients developed a generalized morbilliform rash, which disappeared when the drug was discontinued. One patient developed an acute psychotic episode with paranoid delusions and probably visual hallucinations two days after starting nydrane; it gradually subsided when the drug was discontinued. This patient, however, had electroencephalographic evidence of bilateral temporal lobe dysfunction and showed considerable personality disorder. No other side-effects were observed.

Conclusions

These results differ from those of most comparable series. Merlis and Martin (1956) state that only 3 out of 18 (17%) patients improved as regards frequency of attacks, although 16 out of 18 improved in severity, mainly in respect of post-ictal excitement and confusion. On the other hand, Gotten *et al.* (1951) achieved improvement in 48%. Hawkes (1952) reported 39% improved, 28% worse, and 33% unchanged. Hoenig *et al.* (1956) found 50% improved, 25% worse, and 25% unchanged, and suggest that hydrane is at least

equal in efficiency, though not superior, to the hydantoinates. Robinson (1957) reports a downward trend in the frequency of attacks in 8 out of 11 (73%) patients to whom nydrane was administered over a period of five months. Sharpe *et al.* (1958) found 17 patients out of 25 (68%) improved, 3 (12%) worse, and 5 (20%) unchanged over a period of six months; they noticed an increase in the frequency of attacks during the changeover period. These workers used a dosage comparable to our own.

By contrast, only 3 out of 27 (11%) of our patients showed a sustained improvement, according to the criteria used, 6 (22%) became worse, and 18 (67%) were unchanged. Two others improved temporarily, for two weeks and 24 weeks respectively, the latter ultimately becoming worse than before. Particular benefit has been claimed for patients with temporal lobe seizures, but only one of our patients in this category improved. In only 2 out of 10 patients where nydrane was added to the former treatment did improvement occur; where it was substituted for part of the former treatment only 1 out of 17 improved.

Where nydrane was substituted and deterioration did not occur (11 patients), it may have been responsible for maintaining the former level of control. The improvement in three patients, taken together with the findings of other clinicians and of laboratory experiments, indicates that nydrane probably has some anticonvulsant effect, but from a practical point of view we feel that the results are disappointing and do not justify its use as a routine. On the other hand, occasional patients benefit and relatively few deteriorate, so that its addition may be tried where dangerous amounts of the more established, but more toxic, drugs would otherwise be necessary. It may be useful to try the effect of much higher dosage.

Six patients showed little difference in response whether on active or inert tablets. This is interesting in view of the common finding that many epileptic patients respond temporarily to any new treatment which may be prescribed. In some this is undoubtedly because they take a new remedy with fresh enthusiasm and regularity. In others, however, the benefit may be similar in origin to that obtained by many people from a placebo.

Claims made for the low toxicity of nydrane are upheld by our findings. Two of our patients developed a rash, but no other side-effects were noted. The psychotic episode in one patient did not have a proved relation to the drug. The danger of status epilepticus when changing to nydrane is mentioned by Hoenig *et al.* (1956) and is illustrated by one of our patients; it indicates that the severe case should be admitted to hospital if this procedure is contemplated.

Summary

Nydrane was used in the treatment of 27 patients with severe epilepsy during the routine work of a neurological department: 3 (11%) improved, 6 (22%) were worse, and 18 (67%) remained unchanged.

In six in-patients inert dummy tablets were interchanged with nydrane; no change resulted in the frequency of attacks, unless the dosage of other drugs was altered.

Claims for the low toxicity of nydrane are supported.

On the basis of these findings it is suggested that nydrane is less useful clinically than the more established anticonvulsants; but where exceptionally heavy medication is necessary for control it can occasionally be helpful by reason of its low toxicity.

We thank Dr. Hugh Garland, director of the neurological departments at the General Infirmary at Leeds and Pinderfields Hospital, Wakefield, for permission to make this report on his patients and for his criticism. We also thank Dr. M. J. Parsonage, Assistant Physician to the above departments, for his electroencephalographic assessments. The dummy tablets were provided by Dr. S. Phillips, of the Rona Laboratories, whose help we gratefully acknowledge.

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Medical Memoranda

Partially Treated Meningitis in Infants

Meningitis caused by pyogenic bacteria is always a dangerous disease, especially in infancy. The danger lies in the possibility of early death or of permanent damage to the brain or to the pathways of the flow of cerebrospinal fluid. Early diagnosis is therefore of the greatest importance, but unfortunately is often very difficult. Thus many infants with meningitis are treated empirically at home with sulphonamides without a definite diagnosis being made. This treatment modifies the clinical picture of the illness and may make an accurate diagnosis increasingly complex.

In order to try to demonstrate some of the diverse clinical pictures that can be presented in partially treated meningitis, the following cases are recorded.

CASE REPORTS

Case 1.—A female infant aged 15 months was admitted to hospital on October 9, 1950, with a history of sudden onset of fever eight weeks previously. Apart from the fever, she was irritable, and vomited some feeds. After a six-day course of sulphonamides she improved but remained irritable, had anorexia, and continued to lose weight. The family doctor thought she had pink disease. On admission she was a wasted, irritable baby who resented being handled. She had photophobia but no evidence of infection, no neck stiffness, and no rise in fontanelle tension. Her appearance was that of a baby with pink disease. A lumbar puncture, however, showed a purulent fluid from which *Haemophilus influenzae* was grown. After treatment with sulphadiazine and systemic penicillin for 10 days she rapidly improved, and at the time of discharge was a normal baby. Four years later she was a healthy, intelligent child.

Case 2.—A male infant aged 19 months was admitted to hospital on January 21, 1951, with a history that 18 days previously he had suddenly become febrile and irritable and had vomited some feeds. A short course of sulphonamides brought only slight improvement, and he continued to be irritable and had severe anorexia until the time of admission. When admitted he was ill; temperature 102° F. (38.9° C.). Slight neck stiffness was present, and there was evidence of considerable loss of weight but no other abnormalities. A lumbar puncture showed a purulent fluid, but no organisms

were cultured. After receiving sulphadiazine and systemic penicillin for 10 days he made a good recovery. Five years later he appeared to be a normal child.

Case 3.—A male infant aged 4 months was admitted to hospital on June 2, 1953, with a history that three weeks previously he had become suddenly febrile and irritable, and resented being handled. Over the next two days he had become drowsy and vomited his feeds. He was treated with sulphonamides for several days at home. On admission he was an unwell, wasted baby with a temperature of 100° F. (37.8° C.). There was slight fullness of the fontanelle but no other abnormality. A lumbar puncture showed a purulent fluid from which meningococci were grown. He was treated with sulphadiazine and systemic penicillin for eight days. Progress was satisfactory, and six months later he appeared to be normal.

Case 4.—A male infant aged 15 months was admitted to hospital on November 6, 1953, with a history that five weeks previously he had suddenly become febrile and extremely irritable and had vomited profusely for 24 hours. Sulphonamides were given for several days. There was some improvement, but he continued to be irritable and showed anorexia until his admission. When admitted he was a wasted, irritable baby, with a temperature of 101° F. (38.3° C.). Slight fullness of the fontanelle was present, but there were no other clinical abnormalities. A lumbar puncture gave a purulent fluid from which *Haemophilus influenzae* was grown. Sulphadiazine and chloramphenicol were given for eight days. Progress was satisfactory, and three months later he appeared to be normal.

Case 5.—A female infant aged 8 months was admitted to hospital on November 10, 1953, with a history that five weeks previously she had become irritable and had developed a cold and cough, with marked anorexia. Although some improvement occurred after a six-day course of sulphonamides, she continued to be listless and irritable. Eight days before admission she became drowsy, and a further four-day course of sulphonamides was given. The family doctor thought she had pink disease. On admission she was a wasted, ill-looking baby with a temperature of 101° F. (38.3° C.), but there were no other specific abnormalities and no fullness of fontanelle or neck stiffness. She resembled a case of pink disease so closely that lumbar puncture was not carried out until two days after admission. It showed a clear fluid with 230 cells, 80 mg. of protein, and 37 mg. of sugar per 100 ml., and was sterile on culture. After chloramphenicol and sulphadiazine for nine days she made a good recovery. Two months later she appeared to be quite normal.

Case 6.—A male infant aged 18 months was admitted to hospital on July 19, 1954, with a history that three weeks previously he had suddenly become feverish and irritable and had vomited his feeds. He also had a cold and cough. After sulphonamides for several days he improved, but continued to remain irritable and had anorexia. On admission he was afebrile, showed evidence of considerable wasting, and had slight terminal neck stiffness, but there were no other abnormalities. A lumbar puncture showed a purulent fluid but no organisms were cultured. After sulphadiazine and systemic penicillin for nine days he made a good recovery.

Case 7.—A female infant aged 2 months was admitted to hospital on May 15, 1956, with a history that two weeks previously she had become febrile, irritable, and had vomited her feeds. After sulphonamides at home for six days she had improved considerably, but remained irritable and had anorexia. On admission she had a temperature of 101° F. (38.3° C.), showed wasting, and disliked being handled. Slight fullness of the fontanelle was present, but there were no other abnormalities. A lumbar puncture showed a clear fluid with 517 cells, 70 mg. of protein, and 26 mg. of sugar per 100 ml.; no organism was cultured. She was treated with chloramphenicol for eight days and sulphadimidine for eight days. Progress was good, and when seen one month later she appeared to be quite normal.

Each of these cases also showed a normal *x*-ray picture of the chest, a negative Mantoux test, and normal urine.

COMMENT

These case histories show the alteration in the clinical picture of purulent meningitis in infants treated with sulphonamides. Unfortunately it has not been possible to find the exact dosage that each infant was given, although in each case it was the small dosage normally used for the treatment of minor infection, and the sulphonamides were not given continuously for longer than six days.

Meningitis in an infant nearly always has a sudden onset and should always be suspected in a sudden febrile illness when the following features are present: anorexia and vomiting of feeds; irritability and dislike of being handled; episodes of crying for no apparent reason; and a dulling of the infant's intellect showing itself in a lack of interest in the surroundings.

If untreated, the infant deteriorates rapidly and becomes quite obviously seriously ill within a matter of hours or at least a day or two. When, however, a short course of sulphonamides is given the clinical picture seems to change very considerably. The devastating nature of the illness is altered and the infant continues in a chronic state of ill-health in which irritability and anorexia appear to be the predominant features. Should these symptoms persist over a period of several weeks, as in Cases 1 and 5, the illness in many ways resembles pink disease, and this similarity is so striking that it would be wise always to regard this as a differential diagnosis to pink disease.

Clinical findings of the modified illness consisted essentially of a wasted, irritable baby, often with a slight rise in temperature. Signs referable to cerebral irritation, such as bulging of the fontanelle or nuchal rigidity, were present in only a few of the babies, and then diagnosis was relatively simple. If these signs were not seen the differential diagnosis tended to rest between other conditions presenting this clinical picture of a wasted irritable baby, such as a chronic urinary infection, pink disease, or idiopathic hypercalcaemia.

An interesting and surprising feature of these cases is that, even though the diagnosis is not made until some weeks later, a total recovery seems to occur when energetic treatment is given, and in none of these cases has any neurological sequelae occurred.

In a busy general practice the temptation to treat an undiagnosed febrile illness with chemotherapy is understandable, but I would make the plea that, if chemotherapy is used in such an illness, a non-thecal-passing drug such as oral penicillin should be used rather than a sulphonamide. The diagnosis will then not be obscured.

As medicine advances and more antibiotics are discovered, a distinct possibility arises of many infective disease processes being modified by incomplete treatment: thus it may well be that medical teachers will have to describe not only the clinical picture of an infective disease but its pattern when modified by partial treatment.

I thank the medical and nursing staff of the Children's Hospital, Sunderland, for their care of these infants.

J. B. HEYCOCK, *M.C.*, T.D., M.R.C.P., D.C.H.,
Senior Consultant Paediatrician, Sunderland Area; Associate Physician to the Children's Department, Royal Victoria Infirmary, Newcastle upon Tyne.

Reviews

THE EYE IN EVOLUTION

System of Ophthalmology. Edited by Sir Stewart Duke-Elder. Vol. I. *The Eye in Evolution.* By Sir Stewart Duke-Elder, G.C.V.O., M.A., LL.D., Ph.D., D.Sc., M.D., D.M., F.R.C.S., F.R.C.S.E., F.A.C.S., F.R.A.C.S. (Pp. 843+xvi: illustrated. £6 6s.) London: Henry Kimpton. 1958.

English literature is particularly well served by monographs on special aspects of the comparative anatomy of the eye, such as Lindsay Johnson's atlas on the fundus of mammals, Casey Wood's equally sumptuous study on the fundus of birds, Detwiler's monograph on vertebrate photoreceptors, and the brilliant volumes on the retina and on the vertebrate visual system by Stephen Polyak. More general reviews are contained in Gordon Walls's *Vertebrate Eye* and in the rather textbookish *Comparative Anatomy of the Eye* by J. H. Prince. There is, however, no over-all survey such as Rochon-Duvigneaud's study in French, or the volumes by Pütter and by Franz in German. *The Eye in Evolution* by Sir Stewart Duke-Elder goes far to make up the deficiency. It opens with an extensive section on the effect of light on metabolism, movement, and pigmentation—steps in the emergence of vision. The evolution of the visual apparatus is considered in a systematic and up-to-date survey of both the morphology and function of the invertebrate and the vertebrate eye. The final section of the book deals with evolutionary puzzles, such as the pineal eye, rudimentary eyes, and luminous and electric organs. To facilitate the reading of the text there are many marginal sketches of animals drawn to a uniform size. In all, this is a comprehensive survey, worthy of the rich literature of a fascinating subject.

In the preface Sir Stewart Duke-Elder explains that this book is planned to be the first of 15 volumes of a *System of Ophthalmology* by different hands—this system to replace his own textbook in seven volumes. As it is now some 40 years since an encyclopaedia of ophthalmology in English appeared, and nearly 60 years since an earlier attempt at a systematic survey was made, ophthalmologists throughout the English-speaking world will look forward to the completion of this work. The editor has the profession's good wishes in his formidable undertaking.

ARNOLD SORSBY.

CHRONIC ILLNESS IN BALTIMORE

Chronic Illness in the United States. Vol. IV. Chronic Illness in a Large City. The Baltimore Study. By the Commission on Chronic Illness. (Pp. 620+xxii. 63s.) Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1957.

This is the fourth volume of the reports of the Commission established in 1949 to study the problem of chronic illness in the U.S.A., and the best of the three that I have read. A survey of the relevant literature convinced the Commission there was no reliable information about the morbidity or incidence of chronic disease in the populations of large cities, and with the help of Johns Hopkins Hospital, the Public Health Service, and many other organizations they planned and carried out a systematic survey of a random sample of the inhabitants of Baltimore. The result is a remarkable indication of what may be achieved by the co-operation of medicine and sociology. Persons in hospitals and institutions for the care of the chronic sick were excluded from the survey, and the results refer to the people of Baltimore living in their homes.

The figures are startling. Nearly 1,600 chronic disease processes were identified in each 1,000 of the population, and, of these, 56% were considered to be "substantial." Mental disorders (109 cases per 1,000 population) headed the dismal catalogue, closely followed by heart disease and arthritis; cases of hypertension without involvement of the heart numbered 66 per 1,000. In the preliminary investigation by lay visitors it was found that only one-quarter of the individuals affected were aware of any disability, and this demonstrates the futility of morbidity surveys without adequate clinical investigation. Not unexpectedly most of the "disease processes" were concentrated in the elderly. No woman over 65 years was found to be without at least one of them; on the other hand, in this age group there were 13% of healthy men. Eighty-two per cent. of the children under 15 were free from substantial chronic disease, but in the age group 35–64 this figure had fallen to 34%. In a country in which dentistry has been so well developed it was surprising to find that, after exclusion of the 12% of the population with full dentures, 93% of the remainder required active dental treatment.

An attempt was made to assess the degree of improvement to be expected from adequate treatment. The result was discouraging. Many patients would not accept treatment for conditions of which they were unconscious, and medical treatment of many of the conditions revealed is unsatisfactory. "Only a small percentage (15.1) of the persons disabled for their usual activities was considered to have a potential for improvement." Western civilization clearly has much to learn before its citizens will be healthy.

A. P. THOMSON

THE TUBERCLE BACILLUS

The Bacteriology of Tuberculosis. By Egons Darzins, M.D. (Pp. 488+xii; illustrated. 80s.) Minnesota: University of Minnesota Press. London: Oxford University Press. 1958.

One of the aims of Dr. Darzins has been to summarize the vast literature of the bacteriology of tuberculosis, and his book reads much like an extended review article. The first two parts, occupying almost half its pages, are on the morphology, cytology, sources of energy, and growth of the tubercle bacillus. Part III contains chapters on the collection of specimens, direct smear examinations, culture, and animal inoculation. Parts IV and V are concerned mainly with the typing of tubercle bacilli, atypical mycobacteria, and the use of animals in experimental tuberculosis. Scattered throughout the book are sections dealing with chemotherapy, but they are incomplete, hardly touching on the value or use of different chemotherapeutic drugs or on drug resistance. A further notable omission is the absence of discussion of the nature of immunity or allergy in tuberculosis. There is no review of B.C.G. vaccination or of the epidemiology of tuberculosis.

The arrangement of material is also open to criticism. Though it is adequate in the first half of the book, in the last two parts the author jumps from subject to subject within a chapter for no apparent reason and without a summary of the conclusions that can be drawn. Then, again, some subjects appear in unexpected places: for instance, why include a section on cortisone in a chapter on growth factors for the tubercle bacillus,

when it is well known that the hormone acts on the defence mechanism of the host?

This book can be recommended to a specialist in the field, since for him the 1,600 references from 252 journals will provide a most valuable bibliography. However, he will find it of less value in defining important present-day problems. The clinical bacteriologist may also find the section on diagnostic work of interest, since it describes certain methods that are little known in British laboratories.

D. A. MITCHISON.

REGIONAL ANATOMY

Essentials of Human Anatomy. By Russell T. Woodburne, A.M., Ph.D. (Pp. 620+viii; illustrated. £5.) New York and London: Oxford University Press. 1957.

It is not unusual for an author to ask himself, in the preface of his book, what are his justifications for writing yet another. The justification for the present volume is that the pressure of increasing knowledge in medicine and also in anatomy has been the stimulus for a re-examination of teaching methods in anatomy.

In the first chapter the basic concepts regarding the structure of the various systems are construed in too general a manner to be altogether satisfactory. In the subsequent chapters descriptions are given of the upper limb, head and neck, back, chest, abdomen, perineum, pelvis, and lower limb from a purely topographical point of view. This method is satisfactory for guidance in the study of anatomy in the cadaver, but it fails to give the student an over-all picture of the various systems of the body. The central nervous system is dealt with in only a very sketchy manner in the chapter on the general organization.

In writing a book such as this it is difficult to know what should be left out and what should be included. In many instances too much detail has been given of structures which are relatively unimportant—for example, on pages 78 and 79 there is a detailed description of the branches of the axillary artery, some of which are of very little importance to the student. The illustrations, with few exceptions, are accurately drawn; it is unfortunate that it has not been possible to use colour. Fig. 326 should be redrawn for any future edition, as the size of the prostate gland and trigone of the bladder are out of proportion. In Fig. 329 the ureters open much too high on the bladder wall.

This book will be a useful source of information to students who wish to study anatomy from a regional approach.

W. J. HAMILTON.

THE TEMPESTUOUS TEENS

Journey through Adolescence. By Doris Odlum, M.A., M.R.C.S., L.R.C.P., D.P.M. (Pp. 186. 10s. 6d.) London: Delisle Limited. 1957.

This little book is written for parents and teachers. It is well suited to this audience. Its advice is restrained and its tone is moderate. Dr. Odlum has had considerable experience of adolescent problems, and she writes sensibly about them. Some of the chapter headings will give an adequate indication of the scope of the book: "The Adolescent and the Home," "—and the School," "—and the Job," "—and the Community," "—and Spiritual Values." This was a book worth the writing and worthy to be read.

D. V. HUBBLE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The Care of the Geriatric Patient. Edited by E. V. Cowdry, Ph.D., Sc.D.(Hon.). (Pp. 438. 60s.) St. Louis: C. V. Mosby Company. London: Henry Kimpton. 1958.

Crusader Undaunted. Dr. J. C. Geiger, Private Physician to the Public. By Max S. Marshall. (Pp. 246+viii; illustrated 24s. 6d.) New York, London: Macmillan Company. 1958.

Babies without Tears. A Mother's Experience of the Lamaze Method of Painless Childbirth. By Marjorie Karmel. (Pp. 207 12s. 6d.) London: Secker and Warburg. 1959.

Die Gefässarchitektur der Niere. Untersuchungen an der Hundeniere. By Professor Dr. A. von Kügelgen, Dr. B. Kuhlo, Dr. W. Kuhlo, and Dr. Kl.-J. Otto. (Pp. 111+xi; illustrated DM. 47.) Stuttgart: Georg Thieme Verlag. 1959.

The Psychoanalytic Study of the Child. Volume XIII Managing editors: Ruth S. Eissler, M.D., Anna Freud, LL.D., Heinz Hartmann, M.D., and Marianne Kris. (Pp. 573. 50s.) London: Imago Publishing Co. Ltd. 1958.

Breast Cancer. The Second Biennial Louisiana Cancer Conference. New Orleans, January 22-23, 1958. Edited by Albert Segaloff, M.D. (Pp. 257; illustrated. 37s. 6d.) St. Louis, Missouri: C. V. Mosby Company. London: Henry Kimpton. 1958.

Dal Conscio all'Inconscio nella Veglia e nel Sonno. By Filippo D'Onghia. (Pp. 126. L. 2,000.) Bologna: Cappelli 1959.

Family Influences and Psychosomatic Illness. An Inquiry into the Social and Psychological Background of Duodenal Ulcer. By E. M. Goldberg. With an appendix on Psychological Tests by Victor B. Kanter. Foreword by Eric D. Wittkower. (Pp. 308 +xii. 38s.) London: Tavistock Publications Ltd. 1958.

Plague Fighter. The Autobiography of a Modern Chinese Physician. By Wu Lien-Teh, M.A., M.D.(Cantab.), Mast. P.H. (Johns Hopkins), Litt.D.(Peking), Sc.D.(St. Johns, Shanghai), LL.D.(Hongkong). (Pp. 667+x; illustrated. 30s.) Cambridge: W. Heffer and Sons Ltd. 1959.

Leprosy in Theory and Practice. Edited by R. G. Cochrane, M.D., Ch.B.(Glas.), F.R.C.P.(Lond.), D.T.M.&H. With a foreword by Sir George McRobert, C.I.E., M.D.(Aberd.), F.R.C.P.(Lond.). (Pp. 407+xv; illustrated. 84s.) Bristol: John Wright and Sons Ltd. 1959.

X-Ray Diagnosis of the Alimentary Tract in Infants and Children. By Edward B. Singleton, M.D. (Pp. 352; illustrated. 83s.) Chicago: Year Book Publishers, Inc. London: Interscience Publishers, Ltd. 1959.

Histochemical Technique. By W. G. Bruce Casselman. (Pp. 205; illustrated. 18s.) London: Methuen and Co. Ltd. 1959.

Congrès National des Sciences Médicales. Communications des Invités Étrangers. Bucarest 5-11 Mai 1957. (Pp. 908+viii; illustrated. 51 lei.) Bucharest: Éditions de l'Academie de la République Populaire Roumaine. 1957.

Recent Advances in Respiratory Tuberculosis. By Frederick Heaf, C.M.G., M.A., M.D., F.R.C.P., and N. Lloyd Rusby, M.A., D.M., F.R.C.P. Fifth edition. (Pp. 284+vii; illustrated. 35s.) London: J. and A. Churchill Ltd 1959.

National Academy of Sciences of the United States of America. Biographical Memoirs. Vol. XXXII. (Pp. 457+vi; illustrated. 40s.) New York: Columbia University Press. London: Oxford University Press. 1958.

Practical Dermatology. Second edition. By George M. Lewis, M.D., F.A.C.P. (Pp. 363+xv; illustrated. 56s.) Philadelphia, London: W. B. Saunders Company. 1959.

The Teaching and Learning of Psychotherapy. By Rudolf Ekstein, Ph.D., and Robert S. Wallerstein, M.D. (Pp. 334+xvi. 42s.) London: Imago Publishing Co. Ltd. 1958.

Cancer. Edited by Ronald W. Raven, O.B.E.(Mil.), T.D., F.R.C.S. Volume 5. Part IX. Radiotherapy. (Pp. 406+19+viii; illustrated. 85s.) London: Butterworth and Co. (Publishers) Ltd. 1959.

BRITISH MEDICAL JOURNAL
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STUDENT SUICIDES

Owing to the complexity of the troubles that lead people to commit suicide, and to the fact that they can usually be investigated only in retrospect, we still know too little to take effective preventive action as often as is desirable. This is perhaps particularly true of suicides among university students. The article by Sir Alan Rook in the opening pages of the *Journal* this week is therefore timely, and helps to remedy the shortage of facts that has handicapped the study of these tragic deaths.

It is interesting to find that no apparent difference exists in the incidence of suicide at Cambridge between the period 1928–38 and the most recent decade up to 1958, though a higher rate was found during the 10 years which included the second world war. Student mortality as a whole is most concisely depicted by saying that, of 103 undergraduate deaths in 35 years, 41 were due to accident, 35 to suicide, and only 27 to disease. The figures are similar to those at Oxford which Parnell described[1] when drawing attention to the unexpectedly high incidence of suicide there, and it is evident that the prevention of fatal accidents and suicide would greatly reduce student mortality. The next important fact which Sir Alan Rook appears to establish is that at seven other British universities taken together the suicide rate is much lower than at Oxford and Cambridge, although it is still, so far as can be judged, about twice that for young men of similar age in England and Wales. The rate at University College, London, falls between the rates for the older and newer universities. Suicide rates for women students are generally low.

Sir Alan Rook's contribution and others in the last few years have cleared the ground of a number of misconceptions. Few of the ready opinions expressed as explanations for the high suicide rate have stood up to scrutiny. Ill-fated love affairs, shortage of money, inadequate intelligence, moral perplexity, and the strain of social adjustment that poorer students sometimes experience on arrival at the university—all these have been blamed. No doubt all had figured in individual case histories, but none so far have appeared in more than a small proportion of cases. Among students who become mental patients disharmony between parents and disturbance of relations between the student and members of his family occur rather more often than among controls, but M. A. Davidson and colleagues[2] point out that over half the patients break down in spite of good relationships, and 20% of controls have had similar experience without breaking down.

What factors, then, are clearly recognizable? There are three. First, at least in time, there is a constitutional one, which is brought into prominence by its unwelcome and unexpected association with the current machinery of academic selection at the age of 11 and later. It seems that young men with linear body builds are more liable to suicidal thoughts and more likely to reach a university than are men with other body builds.[3] Secondly, there are work difficulties, with added stress at the time of examinations. Such difficulties may arise from badly organized plans for work, from laziness, excessive outside interests, wrong choice of faculty, illness, or emotional upsets. Occasionally they are primary, and all experienced counsellors know how common the student is who, with an unrealistically high level of aspiration, is encouraged by parental or other pressures to reach for perfection and to regard as failure anything less than first-class honours or life as a Camford don. The formal diagnosis of depression covers many such situations, not only where reasons for reactive depression are assumed to be the cause, but also where absence of any obvious cause earns it the epithet endogenous. The third common factor is sexual adjustment. If, as A. C. Kinsey and colleagues reported,[4] nearly 90% of young men have experienced orgasm by the age of 18, it is not surprising that life *in statu pupillari* should occasionally bring preoccupation with sexual difficulties into prominence: these difficulties relate primarily to finding a socially acceptable solution. Homosexuality is possibly more common in association with suicide than the one case reported from Cambridge might suggest.

Sir Alan concludes his article by saying that there is still need for "more information about . . . the various ecological factors which affect the mental health of undergraduates." Who is to study this problem further, and what techniques are likely to be most fruitful? These are questions which may well be asked at the present time. Should the responsibility rest with the National Health Service, which already undertakes the treatment of the mentally sick? Is the standard of treatment available everywhere as good as it ought to be for

[1] Parnell, R. W., *Lancet*, 1951, **1**, 731.
[2] Davidson, M. A., Lee, D., Parnell, R. W., and Spencer, S. J. G., *J. ment. Sci.*, 1955, **101**, 810.
[3] Parnell, R. W., *Behaviour and Physique*, 1958, London.
[4] Kinsey, A. C., Pomeroy, W. B., and Martin, C. E., *Sexual Behaviour in the Human Male*, 1948, Philadelphia and London.
[5] Skottowe, I., *A Mental Health Handbook*, 1957, London.
[6] Henn, T. R., *Proceedings of the First World Conference on Medical Education*, 1954, London.

these highly selected and important members of the community? If so, are the channels of access to treatment obstructed? I. Skottowe[5] has described what may be and has been done by co-ordinated effort to free them and improve results. Are universities themselves exploring energetically enough the means of preventing mental illness in their midst and the fatalities that stem from it? Meanwhile, more teachers might find some wisdom in the words of a distinguished Cambridge don[6]—namely, to "set the examinations, and the preparations for them, in a fairer perspective before our students and ourselves," for, he added, "who cares in 20, even 10, years' time what class a man has got—except, lamentably, in the teaching professions, whose members for just that reason magnify its importance to their pupils?"

BLOOD-GROUP SUBSTANCES AND GASTRO-INTESTINAL DISEASE

The discovery by Professor I. Aird and his colleagues[1] in 1953 of a significant excess of persons of blood group A among sufferers from carcinoma of the stomach has been followed by overwhelming confirmation of this relationship by numerous workers in many countries. A similar, and even more distinct, relation between duodenal ulcer[2] (and to a less extent, gastric ulcer) and blood group O has also received full and widespread confirmation. Among sufferers from duodenal ulcer there is also a highly significant excess of people who do not secrete ABO (or rather ABH) blood-group substances in the saliva.[3] Other diseases which show a significant excess of people with blood group A among the sufferers are pernicious anaemia, diabetes mellitus, and female genital carcinoma. The subject has been reviewed in these columns[4] and by J. A. Fraser Roberts.[5]

All but one of the diseases mentioned affect the gastro-intestinal tract or its appendages. As, moreover, secretion of blood-group substances by carriers of the secretor gene is almost entirely into the gastro-intestinal tract, beginning with the salivary glands, it is tempting to look upon the presence or absence of the substances in the intestine as directly promoting, or giving protection from, disease. For this reason, among others, much of the work now in progress is concerned not only with secretion of the ABH substances but also with the presence or absence, either on the red cells or in the saliva, of the Lewis (Le^a and Le^b) substances, which have an intimate relation with ABH secretion and non-secretion.[6] Two papers in the present issue of the *Journal* make important contributions to the subject.

Dr. C. A. Clarke and his colleagues describe (p. 603) further work on the relation of blood groups and of secretion of blood-group substances to the incidence of gastric and duodenal ulcers. They show that the effects of group O in contrast to other groups, and of non-secretion in contrast to secretion, in increasing the liability to duodenal ulceration are at least additive and possibly enhance one another. In particular they find that, even among non-secretors, persons of group O are much more liable to ulceration than those of other groups, the differences between the groups being, if anything, greater than among secretors. Since non-secretors have, by definition, none of the substances of the ABH series in their gastro-intestinal fluids, the notable effect of the ABO blood group itself on liability to ulceration cannot be mediated through these fluids.

In the secretions of so-called non-secretors, however, the Lewis (Le^a) substance is nearly always present in considerable amounts,[6-8] and the authors have therefore investigated the total amount of blood-group substances, including those of the ABH series and Le^a. They have done this by a chemical method which, for the purpose, is likely to be much more accurate than serological titration. They have estimated the amount present in the saliva of the simple sugar fucose, which is almost entirely absent from the human body except as a constituent of the molecules of the blood-group substances. They have thus shown that the total concentration of these substances, whether A, B, H, or Le^a, present in the saliva of healthy persons is almost independent of blood group and of secretor status. The average concentration is also almost unchanged in the presence of ulceration, but there is then more variability between individuals than is found between healthy persons; this is perhaps more likely to be the result than the cause of the ulceration.

If the blood group of an individual directly caused or protected from ulceration, it would be expected that in a sibship including both A and O persons there would be a greater tendency to ulceration in the O's. The authors and their colleagues have repeatedly failed to find any significant effect of this kind, and even the relation between non-secretion and ulceration within families, which appeared to be firmly established, is now subject to some doubt as a result of the collection of new data. The most obvious explanation for the apparent discrepancy between the situation within families and that in the population as a whole would be a stratification of the

[1] Aird, I., Bentall, H. H., and Roberts, J. A. F., *Brit. med. J.*, 1953, **1**, 799.
[2] Clarke, C. A., *et al.*, ibid., 1955, **2**, 643.
[3] —— Edwards, J. W., Haddock, D. R. W., Howel-Evans, A. W., McConnell, R. B., and Sheppard, P. M., ibid., 1956, **2**, 725.
[4] Ibid., 1956, **2**, 757.
[5] Roberts, J. A. F., *Brit. J. prev. soc. Med.*, 1957, **11**, 107.
[6] Grubb, R., *Nature (Lond.)*, 1948, **162**, 933.
[7] Brendemoen, O. J., *J. Lab. clin. Med.*, 1949, **34**, 538.
[8] Grubb, R., *Acta path. microbiol. scand.*, 1951, **28**, 61.
[9] Glynn, L. E., Holborow, E. J., and Johnson, G. D., *Lancet*, 1957, **2**, 1083.

population into two strains, maintained distinct by lack or rarity of intermarriage, one with a high frequency of O and a great tendency to ulceration and one with a high frequency of A and less tendency to ulceration. It is, however, exceedingly unlikely that such a stratification exists in every one of the numerous countries where the relation between blood groups and ulceration has now been found, and the problem for the moment remains unsolved.

Since it has thus been shown that liability to duodenal ulcer is unaffected either by the total amount of blood-group substances in the saliva, or by the nature of the secreted substance within the ABH series, Clarke and his colleagues suggest, with good reason, that the most likely mechanism whereby the ABO blood groups and the secretor status affect the tendency to ulceration is an immunological one involving the A, B, H, and Le^a antigens, for these can exist both in a soluble condition in the body fluids and in a fixed state on the red blood cells and in some other tissues. An immunological element in the aetiology of duodenal ulcer should be looked for.

Since the amount of soluble antigens of the ABH series in the plasma is known to be low as a rule (both in secretors and non-secretors), and since there are serious technical difficulties in the way of investigating the small amounts of the Lewis substances which occur in plasma, no deliberate attempts have, it appears, been made to find a relation between disease and blood-group substances in the plasma. It is therefore of great interest to learn of a case (p. 607), studied by Miss M. Barber and Dr. I. Dunsford, in which an extremely high concentration of A substance was found in the serum of a patient dying of carcinoma of the stomach. Most unfortunately there was never an opportunity for examining the patient's saliva for blood-group antigens, but the fact that her red cells were Le (a – b +) makes it almost certain that she was a secretor of A. In the present state of knowledge one can do no more than speculate about a possible connexion between the clinical condition and the serological findings in this case. It will be necessary to examine yet more cases than the 12 tested with negative results by the authors, and perhaps more moribund cases, before it can be assumed that the connexion was other than accidental. It would also, as the authors suggest, be of importance to see whether the histological finding by L. E. Glynn and colleagues,[9] of a high concentration of A substance in gastric cancer cells themselves is a general phenomenon. There is, however, a possibility that the disease was indeed in Barber and Dunsford's case the cause of the high concentration of antigen in the plasma and that further similar cases will be found.

The existence of a connexion between the blood groups, secretion of blood-group antigens, and certain diseases has now been proved beyond question, and must in the long run be of importance in explaining the aetiology of these diseases and in enabling methods of prophylaxis and treatment to be improved. But these practical benefits will not materialize until the underlying nature of the connexions is much better understood than at present. Much further investigation is therefore needed, some of which is at present in progress. We need to know whether secretor status affects liability to carcinoma of the stomach and of the female genitalia, to pernicious anaemia, and to diabetes mellitus. And, for these diseases as well as for gastric and duodenal ulcers, we require much further statistical information on the connexion of the blood groups and secretion with the diseases within families, and in populations other than those originating in Western Europe. Moreover, despite the apparent independence between duodenal ulceration and the composition of the gastro-intestinal secretions, we need to know more about the physiology and biochemistry of the secretion of blood-group substances, and the production of mucopolysaccharides generally, both in health and in disease.

REVIEW OF LOCAL GOVERNMENT

Yet another attempt is to be made to improve local government. The Local Government Commission for England is soon to begin its work by reviewing areas and trying to make local government more "effective and convenient."[1] The first areas of the country to be investigated are parts of the Midlands (including the Birmingham conurbation) and a group of counties bordering on Huntingdonshire. A Local Government Commission for Wales has also been appointed.

The present pattern which separates town and county by distinct and independent administrations dates from the Local Government Act, 1888, and the structure has remained practically unchanged ever since, despite the enormous changes in the functions of local government during that long period. The county boroughs, of which there are 80 in England, are ruled by town or city councils and are what are technically known as "one-tier" authorities, in contrast to the counties, which are "two-tier"—that is, the counties are subdivided into county districts, and the local government functions are allocated between the county and its districts. This has caused much wrangling, as has the constant desire of the county boroughs to enlarge their boundaries at the expense of the counties.

It is admitted by all, save the most partisan, that some counties and county boroughs are too small and the rate yield is too low for the provision of first-class services for their populations, and that some municipal boroughs, which are district councils working under the supervision of the county, are larger and richer than some county boroughs. The problem is complex enough in the provinces, but it is infinitely greater in the London area, and a Royal Commission on Local Government in Greater London is already at work. Special arrangements are also envisaged for the large provincial conurbations.

Examples of small counties, with their populations in brackets, are Radnor (19,130), Rutland (22,730), Isle of Ely (88,880), and the Soke of Peterborough (68,270). Small county boroughs include Canterbury (30,200), Chester (59,100), and Bury (58,210). On the other hand, there are at least a dozen municipal boroughs with populations in excess of 100,000. The other side of the penny is that some local authorities are alleged to be too big and their administration too remote from some parts of their area. Apart from the London County Council, the local government areas with the largest populations are Middlesex (2,250,000), Lancashire (2,110,000), and Birmingham (1,103,300), and those with the largest areas are Devonshire (1,671,388 acres) and the West Riding of Yorkshire (1,785,762 acres).

Though the need for reform has been recognized for many years no political party has had the courage to grasp the nettle. Reform would lose some votes for the party responsible but would attract none. Any attempt to amalgamate a district with its neighbour brings out in full force all whose ambitions for high civic office, such as mayor or chairman of the council of their native or adopted town, would be thwarted ; all the officers who prefer an independent post in a small authority to a subordinate one in a large organization ; and the hosts of private citizens who, despite the fact that they seldom, or never, take the trouble to vote in a local election, passionately resent any change in the rights and privileges of their council as it existed in the days of their grandparents. The turmoil and agitation are akin to those which are aroused whenever a proposal is made to close a local hospital.

The path, therefore, of the recently appointed Local Government Commission is unlikely to be a smooth one. It is to be hoped that their labours will receive a better reward than did those of the Local Government Boundary Commissioners, who produced a comprehensive report[2] in 1947. Their serious attempt to unravel the tangled skein was ignored by the Government of the day. They heard an immense amount of evidence, which, they reported, was based mainly on two themes—a desire of all authorities to extend their area or upgrade their status, and an intention to resist encroachment and to remain undisturbed. If this attitude persists, as it undoubtedly does, there will be little hope of reform. The weaknesses of authorities which are either too small or too large will persist and grow, and the bureaucrats and advocates of centralization will have added ammunition for depriving local government of functions which are rightly administered at the local level.

All this is not so remote from medicine as some would think. Local health authorities have important functions under the National Health Service. The B.M.A. in its evidence[3] to the Guillebaud Committee stressed the disadvantage of tripartite administration. Recommending the establishment of liaison committees and effective cross-representation of the three branches of the profession on the various administrative bodies concerned as the most effective reform in existing circumstances, the Association's evidence went on to state that "such co-ordination could not be fully developed until the inquiry which is being made into the structure of local government has been completed." Reform of local government, however, may mean that the administration will become quadripartite, since some of the present functions of local health authorities will go to county districts, and the hospitals and general practitioners will have two brands of local authority with which to co-operate. Further, the areas of executive councils are broadly those of the present local health authorities, and any change in one will most probably lead to a change in the other. It will be remembered that Sir John Maude, in a reservation to the Guillebaud Committee's Report on the Cost of the National Health Service, expressed the hope that reorganization of local government administration would make possible the transfer of responsibility for the National Health Service as a whole to local administration. He added that such reorganization should have this transfer as "among its principal objectives." Proposals to transfer the whole local administration of the National Health Service to local authorities would be unlikely to find much support in the medical profession, but there is no suggestion that the Government is thinking along these lines, since there is no reference to the National Health Service as such in the regulations under which the commissioners are to work.

[1] *The Local Government Commission Regulations*, 1958, London, H.M.S.O.
[2] *Report of the Local Government Boundary Commission*, 1947, London, H.M.S.O.
[3] *Brit. med. J. Suppl.*, 1954, **2**, 208.

VACCINE AGAINST WORM

Parasitic bronchitis in young cattle, also known as "husk" or "hoose," is a widespread disease causing serious morbidity and heavy mortality in Great Britain and other countries with a temperate climate. The causal organism, *Dictyocaulus viviparus*, a thread-like nematode worm 4 to 8 cm. long, may occur in thousands in the lungs of a single calf in a locality where the disease is highly endemic. Its life cycle is direct—no intermediate host is required—and cattle become infected by swallowing infective larvae on pasture land which in turn is contaminated when larvae produced by the adult worms in the lungs are passed out in the faeces. They develop to infectivity in four days and the whole life cycle takes about three weeks.

It has been known for some time that cattle which recover from parasitic bronchitis have a strong immunity to reinfection, and recently a group of research workers in the University of Glasgow Veterinary School undertook to investigate this immunity and to endeavour to reproduce it artificially. They detected a passive acquired immunity in animals given immune serum intraperitoneally; some degree of active acquired immunity was induced by means of a whole-worm vaccine given intramuscularly. Then outstanding success resulted from the use of a vaccine consisting of living but attenuated infective larvae given orally, a method which had obvious advantages over the previous two and moreover gave a high degree of protection.

The essential part of this new and important technique is the method of attenuating the infective larvae —namely, irradiation with *x* rays before administering them as a vaccine. This treatment permits the larvae to begin their normal migration from intestine to lungs via the mesenteric nodes; here they die, but not before they have exerted the required antigenic effect, in a site where maximum production of immunity would be achieved.

Details of the irradiation of the larvae, dosage, effects, challenge infections, and the results of field trials have been described in recent papers.[1 2] The results have encouraged the Glasgow group to explore the use of larval vaccines in other kinds of helminth infections, and already brief accounts have appeared reporting the success of vaccination of dogs[3] against the canine hookworm *Uncinaria stenocephala* and of calves[4] against the nematode *Haemonchus contortus*. Also under investigation are important helminth parasites such as *Fasciola* species, *Cysticercus bovis*, *Ascaris lumbricoides*, *Metastrongylus apri*, *Dictyocaulus filaria*, *Nematodirus* species, and hookworms.

Immunization against helminth infections has been a subject of much experiment in the past 30 years and an extensive literature has grown up about it. But the concept of controlling helminthic disease by serum inoculation or vaccination has not hitherto been realized in practice, and the protection of man and his domestic stock from some of the more serious helminthic infections still remains a problem unsolved. The discovery and development of a new method of protection are therefore of paramount interest.

[1] Jarrett, W. F. H., Jennings, F. W., Martin, B., McIntyre, W. I. M., Mulligan, W., Sharp, N. C. C., and Urquhart, G. M., *Vet. Rec.*, 1958, **70**, 451.
[2] Jarrett, W. F. H., Jennings, F. W., McIntyre, W. I. M., Mulligan, W., and Urquhart, G. M., *Proc. roy. Soc. Med.*, 1958, **51**, 743.
[3] Dow, C., Jarrett, W. F. H., Jennings, F. W., McIntyre, W. I. M., and Mulligan, W., *Vet. Rec.*, 1958, **70**, 999.
[4] Jarrett, W. F. H., Jennings, F. W., McIntyre, W. I. M., Mulligan, W., and Sharp, N. C. C., ibid., 1958, **70**, 978.

REGULATION OF SOFT DRINKS

A report[1] by the Food Standards Committee discusses the need for regulations governing the composition of soft drinks, and contains recommendations for revision of the present regulations. The national expenditure on all classes of soft drinks has greatly increased since 1939, and now amounts to about £100m. per year. The committee considers that these beverages have little nutritional value, and its main concern is that the customer should get fair value for his money. Fruit drinks should really contain fruit, and their sweetness should depend on the presence of sugar, not saccharin. Labelling should give an honest account of the nature of the product, with a clear statement of the percentage of fruit or juice which it contains. "Glucose beverages," for which there have been special regulations in the past, should in future be subject to the same rules as other drinks, as they are held to have no special virtue from the medicinal point of view.

Suggestions are given for minimum standards of composition which must be attained before drinks can be sold under various descriptions, such as squashes, fruit drinks, barley drinks, tonic waters, and soda water. To the inexpert the amounts of fruit demanded may seem surprisingly small. Thus a citrus fruit squash, made by pressing the fruit, need only contain 5% (vol./vol.) of juice if it is intended for drinking without dilution, or 25% if water is to be added. For citrus fruit drinks, made by the comminution of the whole fruit followed by straining, the requirements are even lower, at 2% and 10% for consumption without and after dilution. For fruit squashes, other than citrus, the level of 10% is considered to be adequate even if the squash is to be diluted. Indian and quinine tonic waters will differ from all other beverages in being allowed to contain saccharin, presumably because an excess of sugar reacts unfavourably to the addition of gin. The standards for quinine in these drinks is to be 57 parts of quinine sulphate per million: sugar must reach 4½% (wt./vol.), and saccharin must not exceed 80 parts per million. Soda water is to contain 570 p.p.m. of sodium bicarbonate.

The enforcement of the regulations will be backed by the public analytical services, and research on suitable methods of analysis is to be encouraged. No tests will be made, however, of the preservation of the vitamin C originally present in the fruit, since it is accepted that most of it will be lost. Thus a teaspoonful of the orange juice distributed under the Welfare Food Scheme contains at least 10 mg. of vitamin C, whereas a one-third of a pint bottle (190 ml.) of ready-to-drink comminuted orange drink may contain as little as

[1] Ministry of Agriculture, Fisheries, and Food. Food Standards Committee, *Report on Soft Drinks*, 1959. H.M.S.O., London. Price 1s. net.
[2] See annotation, *Brit. med. J.*, 1954, **1**, 510.

1 mg. The report does not mention artificial colouring agents, which are presumably covered by regulations generally applicable to all foodstuffs, nor stimulants such as caffeine in drinks of the "cola" type. The idea that highly acid soft drinks may harm the teeth is discounted on the grounds that their contact with the teeth is of short duration, and the use is to be allowed of citric, tartaric, and malic acids in manufacturing fruit drinks, and of lactic, acetic, and phosphoric acids for other soft drinks. As a general principle the composition of the drink must be clearly stated on the label.

From the medical point of view the committee's most important decision is perhaps its denial that glucose, the form of sugar present in the blood, has any advantage over cane sugar in beverages mainly intended for invalids. In a letter published elsewhere in this issue (p. 646) Dr. A. H. Douthwaite suggests that this part of the report should alert the medical profession "to any possible extension of condemnation of glucose or liquid glucose in therapeutics." The committee's decision was taken after consultation with the Committee on Medical and Nutritional Aspects of Food Policy. A ban is proposed on advertisements which make any special claims for the virtues of glucose and on advertisements of a medical or pseudo-medical character based on recommendations from the medical and nursing professions or testimonials from individual purchasers.

ABORTION ON T.V.

On the B.B.C. television programme "Lifeline" last week a psychiatrist, a gynaecologist, and a forensic pathologist discussed for half an hour the question of abortion. Two girls describing their own illegal abortions, at the hands regrettably of doctors, was the lead-in to pin viewers to their screens. Anatomical charts were used to illustrate the operations, and the programme began and ended with a long cool look at a three-month human foetus. Apart from its intrinsic attraction for viewers, the foetus was there to reinforce the medical team's basic tenet—that abortion at the third month or later involves "the deliberate destruction of a miniature human being who has a right to live." All the contributors were anonymous. The only view of the two girls was the backs of their heads.

What did the viewing public learn from this programme? Put briefly, viewers were told the law on abortion; and were informed that termination at the third month even when done legally in good circumstances can be dangerous and lead to long-lasting complications; that the incidence of criminal abortion is appallingly high (estimated at 150 a day in Great Britain); that the conditions under which criminal abortions are done are usually shockingly squalid; and that some people would like to legalize abortion after rape and incest, rubella in early pregnancy, and if there is a serious threat of suicide—though on this last count the psychiatrist recorded his disagreement.

This was a good attempt at preventive medicine and a good subject for it, for in Britain to-day criminal abortion is a major social evil. One may deplore the unnecessarily "dramatic" lead-in: the incidence figures, well handled, would have been quite enough to jerk the most complacent viewer into attention. The gynaecologist's account of the complications of therapeutic abortion cannot have been very comforting for those about to undergo it, nor were the remarks later on about the risks of maldevelopment after rubella without their danger. When a doctor agrees to appear on television he assumes a responsibility that should make him weigh beforehand each word, each nuance of expression, especially carefully. There must be the highest standard of anticipation of viewer response. On rubella in pregnancy anticipation was below what it should have been. These criticisms apart, the programme was sensible and unemotional—and useful. Little advantage, however, was taken of the visual medium—just the projection of the foetus and the anatomical charts. In fact, except for this, it could all have been done equally well on the old steam radio—perhaps even better, if the medical speakers were really meant not to be recognized.

BRITISH BOOKS ABROAD

We have often commented on the excellent work done by the medical department of the British Council and lamented the niggardly budget which prevents expansion of the Council's highly successful efforts to increase the prestige of British medicine abroad.[1] We are glad, therefore, to see from the latest White Paper[2] on the overseas information services that the British Council's grant is to be substantially increased. The White Paper states: "The largest single factor common to the many and varied countries of Asia and Africa is the desire for education." Unfortunately over the past years there has been a deplorable lack of initiative in Government departments to overcome the difficulties of countries which could not afford to buy British books and periodicals because of currency restrictions. In describing the famine of British printed matter in Turkey, India, and Pakistan, we have already pointed out in these columns how, to give one example, the U.S.A. has ensured through subsidies that American textbooks and periodicals are at the disposal of a world longing for information.[3] Now, thanks in part to Dr. Charles Hill's recent visits to countries in Asia and Africa, more books are to be supplied to British Council libraries and more money will be spent on presenting books to universities and other libraries. A pilot scheme has been devised to enable some students to borrow books for the duration of their course of studies. Even so, the White Paper admits that these arrangements, admirable as they are, will by no means meet the needs of all those many thousands of students who want British books which they cannot afford. "The Government are studying ways of encouraging the flow of British publications overseas," states the White Paper. The flow must become a flood if the world's thirst for knowledge is to be quenched.

[1] *Brit. med. J.*, 1957, **2**, 1228.
[2] *Overseas Information Services*, 1959, H.M.S.O., London. Price 6d. net.
[3] *Brit. med. J.*, 1957, **2**, 281.

Drug Treatment of Disease

MIGRAINE: PART II*

BY

RAYMOND GREENE, M.A., D.M., F.R.C.P.

Senior Physician, Royal Northern Hospital and New End Hospital, London

DRUGS TO REDUCE FREQUENCY AND SEVERITY OF ATTACKS *(cont.)*

5. Hormones

As one would expect, there is hardly a hormone which has not been tried in migraine or which has failed to elicit laudatory claims. Cortisone is sometimes useful to offset the nausea induced by ergotamine, but otherwise the only hormones which may be expected to be helpful are the progestogens, and these only in one type of the disease—premenstrual migraine. Their use in this fairly common form of migraine has been fully described by Greene and Dalton (1953). In brief, if attacks of migraine occur consistently at the time of ovulation or during the last 10 days of the menstrual cycle or both, progesterone should be given intramuscularly in a dose of 25 mg. or more on alternate days for a week before the expected attack. The injections are continued until the day before the expected onset of menstruation. The treatment is successful in about 80% of cases, but it is often necessary to repeat it regularly month by month. Experiments are now in progress to determine whether 19-norethisterone, which is active when given by mouth, may be used to replace parenteral progesterone. Ethisterone (10 mg. three times a day by mouth) has been found beneficial in a minority of cases.

The mechanism of action of progestogens is still uncertain. The current hypothesis, which does not account for all the facts, is that an unduly high oestrogen: progestogen ratio, present at the time of ovulation and in the premenstrual phase, induces retention of water, perhaps by causing retention of sodium. The water retention causes sufficient cerebral oedema to act as a "trigger" in women in whom a constitutional tendency to migraine is present.

6. Antihistamine Drugs

Histamine, a powerful vasodilator, can cause headache in healthy people by dilating the cranial arteries, and it appears that some patients are peculiarly sensitive to histamine. Some physicians have held that the dilatation of the cranial arteries which accompanies the painful phase of migraine is a "histamine effect," and in consequence many antihistaminic drugs have been tried in this affliction, and isolated successes have been reported. I am not aware of a large controlled trial. The antihistamine drugs are very numerous and cannot all be described here.† Their hypnotic properties are a disadvantage when treating this type of headache.

7. Histamine and Neostigmine Desensitization

Histamine desensitization can be achieved by the subcutaneous injection of gradually increasing doses, but it has not been conclusively proved that the method has prophylactic value in true migraine, and it is troublesome to carry out. Similar doubts arise in considering the procedure of neostigmine desensitization, which is based on the hypothesis that the arterial dilatation is due to acetylcholine. As neostigmine inactivates cholinesterase, the injection of gradually increasing quantities might accustom the body to the action of acetylcholine. The value of the method remains questionable. Desensitization to specific allergens has, perhaps, a sounder foundation, but is also of unproved value.

8. Miscellaneous

All or almost all the vitamins, thiocyanate, calcium, potassium perchlorate, belladonna, and numerous vasodilators and vasoconstrictors have been suggested. It is noticeable how often an author has described his success in a few cases and has failed to publish later the results of a more extended trial. "Let us use these new drugs while they still work." Of late, hydantoinates such as phenytoin sodium B.P. ("epanutin") have been tried, but I have heard of no controlled investigation and have no experience of them.

DRUGS WHEN AN ATTACK THREATENS

1. Analgesics

Migraine is not invariably accompanied by severe pain, and in mild cases satisfactory relief may often be obtained by the use of common analgesics such as aspirin and amidopyrine. It is hardly ever justifiable to use more powerful analgesics such as pethidine or opium alkaloids. Migraine is a not uncommon cause of drug addiction.

2. Barbiturates

Even in more severe attacks, barbiturates may be useful, especially for their capacity to allay the accompanying fear. Many patients find "veramon," a combination of amidopyrine, 286 mg., with barbitone, 114 mg., an excellent remedy, but the danger of agranulocytosis from amidopyrine, uncommon though it is, must not be forgotten.

3. Hormones

Progesterone, so valuable as a prophylactic in true premenstrual migraine, is useless in the treatment of an acute attack. On the other hand, cortisone, which is both useless and, because of its side-effects, inadvisable as a prophylactic, may in an occasional case entirely abort an attack. It should be given by mouth at the very beginning in a dosage of 50 to 200 mg. If vomiting is an early symptom it may be given intramuscularly.

*Part I appeared last week; Part II concludes the article.

†The pharmacology of the antihistamines was reviewed by Professor J. H. Burn, F.R.S., in an earlier article in this series (*Journal*, October 4, p. 845).

Even when it fails to prevent headache, it may reduce the nausea and vomiting caused by ergotamine. A.C.T.H. (25 to 100 mg. by injection) has a similar effect, which is slower in onset but more durable.

4. Miscellaneous

An immense variety of measures has been claimed as beneficial for some patients. In our ignorance of the initiating mechanism in the majority of patients, it is justifiable to try them one by one if better-attested methods have failed. Such are nicotinic acid (25 to 100 mg.), antihistaminic drugs (see above), including dimenhydrinate (50–100 mg. by injection), chlorpromazine (see above), inhalation of oxygen, the injection of procaine in the neighbourhood of the most painful area, nitroglycerin (0.3 mg.), amyl nitrite inhalations, and counter-irritants applied to the scalp. It is probable that the effect of most of these measures may be ascribed to the comforting feeling that something is being done.

5. Ergotamine Tartrate

Ergot remains the most important drug in the treatment of the acute attack.

In a small proportion of cases, ergotamine tartrate tablets, 2 mg., given very early in the attack, and repeated hourly to a limit of 10 mg., may confine the attack to the phase of vasoconstriction, the relatively tolerable phase. The patient is required, and indeed prefers, to remain recumbent in a dark room, preferably alone and free from the fussing of solicitous relations. Unfortunately, the dose needed to abort the pain is too often high enough to cause toxic effects, which to many patients are more unpleasant than an untreated attack. These are nausea, vomiting, muscle cramps, an ineffable feeling of prostration, and sometimes a phobia for the drug itself. These effects may, in some patients, be prevented by the administration (if possible even before the ergotamine) of atropine, dimenhydrinate, or chlorpromazine. Prednisolone may be extremely useful, given by mouth or, if vomiting has begun, by injection, in doses of 5 mg. to 25 mg. Some patients find that dihydroergotamine, of which about double the dose of ergotamine is needed, is better tolerated. Whichever drug is used, an effort should be made to find the minimum dose which will prevent or alleviate the headache without production of side-effects.

Ergotamine tablets are the simplest but least reliable of the preparations available. In such cases, one of the available combinations with caffeine may be tried, as described above. Other patients will require rectal suppositories (2 mg. with or without caffeine), which are often more reliable and produce side-effects in fewer patients. Severe cases usually need parenteral administration, and patients should be taught how to give the injections to themselves. It is remarkable that, though no doctor would think of treating a diabetic without teaching him the technique of injecting insulin, few make the effort when migraine is the complaint. Ergotamine tartrate is supplied in ampoules of 0.25 mg. in 0.5 ml. and may be given subcutaneously by the patient or intravenously by the doctor in emergency. But, if a doctor has to be sent for, the administration is usually too late. Again, the minimal effective dose should be found by trial and error. The dose may be repeated after an hour or two, but not more than 1.5 ml. of ergotamine tartrate or 3 ml. of dihydroergotamine methanesulphonate should be given in a day.

The contraindications to the use of ergot have been given in the description of its prophylactic use. One point should be added: the over-frequent use of ergotamine has been known to increase the frequency of attacks. It should be used as rarely as possible and in the minimal effective dosage.

The very success of ergotamine treatment in a high proportion of patients has its dangers. It is all too easy for the overburdened general practitioner to teach his patient the technique and thereafter to confine his activity to the prescription of further supplies. The disorder needs close supervision if an increase in the frequency of the attacks and the onset of chronic ergot poisoning are to be avoided. Even when the general measures outlined at the beginning of this paper have failed greatly to reduce the frequency and severity of the attacks, they should never be allowed to sink into the background of the doctor's or the patient's mind. Without them drugs are merely props.

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PERSONAL MEDICAL RECORD DISKS

BY

H. J. PARISH, M.D., F.R.C.P.Ed.

Clinical Research Director, Wellcome Research Laboratories, Beckenham, Kent

The need for a personal system of recording diseases contracted, idiosyncrasies and the like, blood group, and all preventive inoculations is often mentioned in medical literature. Such a record should ideally be carried on the person: it should be shown to the doctor on request, and in certain circumstances he should look for it. The availability of the immunization history may obviate unnecessary inoculations, and may be of assistance in making a diagnosis. The record would also ensure speedy identification in cases of accident, sudden coma, or other emergency.

Cards and Other Methods of Recording

Various record cards, commonly made of cardboard, have been issued by certain commercial firms and hospitals, but have the disadvantage that they become dirty and tattered when carried in ordinary wallets or handbags. If such cards are made of plastic material or kept in plastic envelopes (which is seldom done) they should remain clean and intact much longer, and this would be a step in the right direction. An alternative procedure to carrying the records on the person is to put them away in a safe place at home; but this has the drawback that they may not be produced quickly enough to prevent an unnecessary injection of, say, tetanus antitoxic serum (Tet/Ser) for someone who has already been fully immunized with tetanus toxoid (Tet/Vac). All aspects of the prevention of tetanus in injured persons have been discussed by Parish, Laurent, and Moynihan (1957) and by Parish (1958).

Tattooing has also been suggested, mostly facetiously, for the more important inoculations and other records, but this would certainly be impracticable for repeated entries, with dates—for example, reinforcing doses of tetanus toxoid or smallpox vaccine (Var/Vac).

If tattooing, whereby the record is permanently "fixed" to the body, is out of the question, can some system of

recording be devised which would be less likely to get separated from the patient than cards, and also be more durable? A locket containing the necessary information has sometimes been suggested (*South African Medical Journal*, 1958). Another possible solution would be a return to the old wartime identity disk, worn on a bracelet or necklace (Elias-Jones, 1958).

The Three Disk Method

The use of three thin disks (about the size of a florin) of a base metal, on a swivel, is now being investigated. These provide four inner surfaces for notes, and have the merit of being neater and stronger than a locket: a locket clasp does not have to be opened, and there are no hinges to be broken or strained. The information is engraved on the disks, and is readily accessible. There is a hole through the swivel attachment, through which a nylon or other cord or chain can be threaded, for wearing as a locket or pendant. Alternatively—as, for example, when a schoolboy does not wish to be thought effeminate—the disks can be carried (without any attachment) with a person's money in a pocket, purse, wallet, or handbag. They may also be attached for convenience to a key-ring or incorporated in a wrist bracelet. If desired, the two outer surfaces of the disks may have some ornamentation—for example, a religious emblem or the owner's initials.

FIG. 1. — Disks closed.

The following particulars could usefully be engraved on the disks:

Face 1.—Name, address, date of birth, national insurance number. (In the event of change of address, the single disk concerned could be replaced.)

Face 2.—Blood group, including Rh (top left segment of disk); important idiosyncrasies or diseases from which he might be known to suffer, such as allergy to serum or penicillin, haemophilia, epilepsy, diabetes, porphyria (top right segment of disk); infectious and other diseases contracted, operations.

Face 3.—Injections of toxoids, vaccines, tuberculins, antisera, etc. (Records of injections of tetanus antitoxin and other antisera are obviously important.) The abbreviated titles for serological products proposed by Perry and Parish (1956) and adopted by the *British Pharmacopoeia 1958* are convenient and readily interpreted in any part of the world. With the increasing prevalence of long-distance travel, this code-scheme should be employed on an international basis.

With regard to the recording of dates, it is considered necessary to include only the year and the month, but not the day of the month. Thus, 57/5.5.6 would indicate two injections in May and one in June, 1957. The omission of the day leads to a considerable economy of space.

The accompanying photographs illustrate a typical record. It will be seen that only three of the four internal surfaces of the three disks have been used, and that there is still a fourth surface for subsequent records. One entry (Dip/Vac 53/8) calls for special comment. This was a reinforcing dose of diphtheria prophylactic, but the child's record card, from which the information was copied, did not specify the variety of preparation: it was probably P.T.A.P. (Dip/Vac/PTAP).

A decision has not yet been reached on the most suitable metal or other material for the manufacture of the disks. The first samples of gilded base metal were provided by Messrs. A. Walker and Son, Jewellers and Silversmiths, 31, High Street, Bromley, Kent. The engraving is very legible, and the disks are wearing well. Research is in progress on other types of metal or light plastic material, and also on other and simpler methods of engraving. At present, it is uncertain who should organize and be responsible for the transfer from cards to disks, and how often this should be done. Perhaps the onus should rest primarily on public health departments, in collaboration with the schools, although the co-operation of hospitals and private practitioners is also important. At the time of school entry, when a child first becomes separated from its parents, the need for record disks first becomes apparent.

With modern developments in photography, all personal medical records could readily and cheaply be reproduced in convenient size, as a safeguard against loss of disks or record card.

How Record Disks Would Help

In a case recorded in Canada (Toogood, 1958) a young girl developed tetanus after a wound. Tetanus antitoxin was not given prophylactically because the mother said that tetanus toxoid immunization had been carried out. "On checking on the available records it was eventually possible to establish the fact that a primary course of tetanus toxoid immunization had, in fact, been refused by the child's grandmother at a time when the child was not resident in the parents' home, and that she therefore was a non-immunized individual." Fortunately the girl recovered.

Dr. Laurent has informed me of two cases where the lack of documentary evidence of previous inoculations might have led to serious consequences. A girl of 13 was admitted to Hither Green Hospital with mild tetanus and a verbal history that she had been previously immunized with "triple vaccine." As the disease was already established, she was given tetanus antitoxin and not toxoid. It transpired later that the doctor had immunized her with diphtheria-pertussis vaccine, without any tetanus toxoid as alleged. A scar over one knee elicited a history of her having had an operation at another hospital following a street accident three years previously; the mother did not know whether or not tetanus antitoxin had been given at that time. Six days later it was confirmed that she had indeed received tetanus antitoxin. Fortunately this patient was given therapeutic tetanus antitoxin

FIG. 2.—Obverse faces of disks.

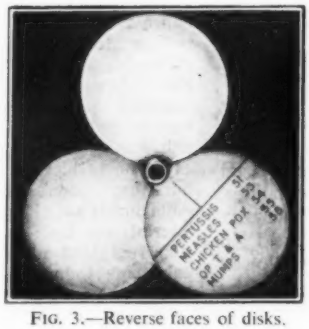

FIG. 3.—Reverse faces of disks.

intramuscularly before an intravenous dose. She made a complete recovery from the infection, but had an attack of serum sickness.

A member of the hospital domestic staff stated that she was sure that she had been vaccinated against smallpox and, as evidence of this, showed a small circular scar over one deltoid. On further inquiry, it was found that this was a scar of a B.C.G. vaccination and that she had never been vaccinated against smallpox; she thought the two procedures were the same.

These examples could easily be multiplied. Statements made by patients or relatives are of doubtful reliability, and are therefore often disregarded by the doctor, who plays for safety—for example, by giving tetanus antitoxin to accident cases that are already actively immune.

Conclusion

The record disks described are an improvement on the card system of recording essential information about immunization, etc. While some disks would certainly be lost, others would be carried on the person and have a long, effective, and useful life.

The method is adaptable. The disks can be made of many different types of material from gold to base gun-metal, or some variety of plastic. They may be worn round the neck, on a nylon cord; they may also be incorporated in a locket or a wrist bracelet; they may be carried on a key-ring, or with a person's money, either loose in the pocket or in a purse or wallet.

A mechanism whereby engraving can be done without too much inconvenience and expense is desirable, although, of course, the latest information may be recorded on duplicate record cards till a suitable opportunity for etching occurs.

My thanks are due to Dr. L. J. M. Laurent for illustrative examples of the need for records, and to Mr. E. A. Jones for the photographs.

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OEDEMA AND ITS CONTROL

[FROM A SPECIAL CORRESPONDENT]

The clinical effects of electrolyte disturbances were discussed at a conference held at the Royal College of Physicians in London on February 27 and 28. This was the second of a series of symposia arranged by the College for its members and fellows who are engaged in consulting medicine or pathology, and the proceedings of this one are soon to be published in full. Topics for discussion covered physiology of electrolytes, body "spaces" and practical techniques, factors that control electrolyte balance, and clinical conditions such as diabetic ketosis, gastro-intestinal diseases, and renal disorders, which may induce electrolyte abnormalities. The opening speakers, as the President, Professor ROBERT PLATT, pointed out, were all actively engaged in investigating the topic they introduced, and this allowed spirited discussion and from time to time healthy hypothetical speculation.

Volume Receptors

One session was devoted to oedema and its control. Professor G. M. BULL pointed out that despite its many different aetiologies the ultimate cause for the collection of excess fluid in the body was increased renal tubular activity leading to retention of sodium, chloride, and water. The osmolarity of the body fluids was largely controlled by retention or excretion of water, and this was effected by the osmoreceptors; these, when bathed by a hypertonic solution, stimulated the neurohypophysis to excrete increased amounts of antidiuretic hormone, with consequent retention of water by the kidney. Conversely, any tendency to hypotonicity was countered by diminished secretion of antidiuretic hormone and elimination of water. What still remained to be explained was the mechanism for regulating the total volume of fluid in the body, because the infusion of isotonic fluid, which had no effect on the osmoreceptors, was promptly followed by a diuresis to restore the extracellular volume of fluid to normal.

Professor Bull then developed his hypothesis that the control of the amount of fluid in the body was dependent on volume receptors: these, by various humoral mechanisms, such as regulating the secretion of aldosterone by the adrenal cortex and thus influencing the renal tubular reabsorption of sodium, and perhaps also by neural mechanisms, controlled the renal elimination of salt and water. The finding that sequestration of fluid in the legs by the application of cuffs to the thighs led to retention of fluid suggested that the volume receptors were located in the vascular compartment, and this was in keeping with the observation that fluid was retained when a normal subject stood up after lying down. The volume receptors did not seem to be influenced directly by the cardiac output, because oedema developed in heart failure with a high output, as occurred in pulmonary heart disease. Nor was there evidence that the volume receptors were influenced by changes in the oxygen or carbon dioxide content of the blood. There was, however, some early experimental work to suggest that the volume receptors were located in low-pressure areas of the circulation, such as the auricles, and that they were activated by pulsatile, rather than static, pressure changes.

More experimental work is needed to prove this hypothesis, which would begin to explain why the kidneys retain salt and water in such widely diverse conditions as hepatic cirrhosis, in which as a result of hypoalbuminaemia and increased portal venous pressure fluid is sequestrated in the peritoneal cavity, and cardiac failure due to mitral stenosis.

Diuretics

Dr. A. G. SPENCER then discussed diuretics, and emphasized three principles governing their use. First, they provided only symptomatic treatment, and treatment of the underlying disease responsible for the oedema must not be neglected. Secondly, diuretics were effective only when renal blood flow and glomerular filtration rate were adequate. Thirdly, they might induce electrolyte disturbances.

Digitalis and theophylline exerted their diuretic effect largely by increasing the glomerular filtration rate through improvement in the cardiac output, and so providing more sodium for excretion by the tubules. Mersalyl and chlorothiazide inhibited reabsorption of sodium and chloride, and the resultant diuresis was an osmotic consequence of this. Urea induced a diuresis by osmosis without primarily influencing sodium reabsorption. Carbonic anhydrase inhibitors, such as acetazolamide, increased the excretion of bicarbonate and hence sodium and potassium, but they were self-limiting in their short-lived effect. Antagonists of aldosterone were of considerable scientific interest, but their relatively weak effect when given alone suggested that aldosterone was not so all-important in enhancing sodium retention by the renal tubules as some had supposed. Professor F. T. G. PRUNTY pointed out later that, even if not a powerful diuretic, "spirolactone"

was a most useful tool in confirming the diagnosis of primary aldosteronism (Conn's syndrome).

Chlorothiazide and Hydrochlorothiazide

Dr. R. I. S. BAYLISS discussed the action of chlorothiazide and showed that its principal effect was to enhance the excretion of sodium and chloride, and that it seldom gave rise to hypochloraemic alkalosis, which occurred more readily with mercurial diuretics and was often responsible for mersalyl resistance. In addition, chlorothiazide had a slight carbonic anhydrase inhibitory action, and this was responsible for some increase in potassium excretion. Apart from this tendency to induce potassium depletion, which led to enhanced sensitivity to digitalis, and which could readily be avoided by intermittent dosage and potassium supplementation when treatment was prolonged or appetite poor, chlorothiazide was singularly devoid of side-effects or toxicity. Some cases of nausea and rashes had occurred; purpura due to thrombocytopenia had been observed on occasion, and one case of agranulocytosis had been reported, but, important though these manifestations were in the individual patient, they could not be considered significant in relation to the very large number of patients who had been successfully and uneventfully treated. Chlorothiazide had the great advantage that it was effective and could be given by mouth.

The recently developed derivative hydrochlorothiazide was, weight for weight, more potent than chlorothiazide, but this was not necessarily an advantage unless it had some qualitative difference in its diuretic effect. It was shown that in normal subjects the hydro-compound was 10 to 12 times more potent than chlorothiazide, but in oedematous patients the ratio varied from less than 10 times to more than 20 times more potent. Qualitatively it was difficult to detect any difference between the two. Since hydrochlorothiazide also increased excretion of potassium and bicarbonate, the same precautions in its use should be applied as with chlorothiazide.

EPSTEIN'S BRAIN

"I am a speaking likeness of a bust by Epstein," said Sir Russell Brain at a dinner in his honour at the Royal College of Physicians of London on March 2. Sir Jacob Epstein, who was at the dinner with Lady Epstein, unveiled the bronze bust in the Library after dinner.

Bronze bust of Sir Russell Brain presented by the Fellows of the Royal College of Physicians.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Decadron (Merck Sharp & Dohme).—This is dexamethasone (16α-methyl 9α-fluoro prednisolone), available in tablets containing 0.5 mg.

Dexa-cortisyl (Roussell).—This is dexamethasone acetate, available in tablets containing the equivalent of 0.5 mg. dexamethasone.

This is the most recent addition to the synthetic steroids. It is about 7½ times as effective as prednisolone in suppressing the inflammatory reaction, and the earlier reports claimed that it was relatively free from undesirable side-effects. More recent work suggests that these claims were made prematurely.

Although dexamethasone does not cause retention of sodium, its administration can lead to an increase in cellular katabolism, and the resulting urinary losses of potassium and nitrogen are of a similar magnitude to those induced by doses of prednisolone which have a comparable anti-inflammatory effect. It appears, moreover, that dexamethasone does not differ significantly from the older steroids in its effects upon carbohydrate metabolism and gastric secretion, and that it is equally likely to produce adrenal suppression.

Theoretically it might be used, as an alternative to one of the older preparations, in any condition which will respond to the administration of steroids in pharmacological doses. Initially 1.5 to 4.5 mg. of the drug is given daily in divided doses. When the desired effect has been achieved, the daily dose may be reduced gradually to zero. The duration of therapy will, of course, depend on the underlying condition.

The same contraindications apply to the use of dexamethasone as to the use of prednisolone. In addition, dexamethasone should not be given to patients suffering from hypercalcaemia, as it has been shown to raise the level of the serum calcium. The superiority of dexamethasone over the older steroids has still to be assessed by more adequate controlled tests.

N.H.S. basic price: decadron, 100 tabs., 76s.; dexa-cortisyl, 100 tabs., 76s.

Vallergan (May and Baker).—This contains the neutral tartrate of trimeprazine, 10-(3-dimethylamino-2-methyl-propyl)-phenothiazine. It is available in tablets of 10 mg., syrup of 2 mg. per ml., and forte syrup of 6 mg. per ml. Like the related phenothiazine derivatives chlorpromazine and promethazine, it has a strong central sedative action. It is also a powerful antihistamine and anti-emetic substance, and has spasmolytic activity. It does not possess the anti-adrenaline properties shown by chlorpromazine.

As an antipruritic drug it may be given in divided doses, preferably after meals. The amount required by each patient should be carefully determined, and is usually 10–40 mg. a day for adults. Its action begins after about 1 hr. Its sedative properties should be borne in mind if it is given to ambulant patients who may drive vehicles or handle machinery.

For anaesthetic premedication of children, the forte syrup may be given 1 hr. before anaesthesia; doses from 0.5 to 2 mg. per lb. (1–4 mg. per kg.) body weight have been recommended, depending on the degree of sedation desired. Atropine is also needed.

The phenothiazines are powerful and potentially toxic substances, and their effects should be closely watched. They have caused dizziness, depression, excitement, fainting, and dermatitis as well as the usual drowsiness and dryness of the mouth.

N.H.S. basic price: 50 tabs., 6s. 4d.; 4 fl. oz. syrup, 4s. 2d.; 4 fl. oz. forte syrup, 8s. 4d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Invalid Vaccination Certificates

SIR,—In the course of my duties a large number of international certificates of vaccination against smallpox are submitted to me. It is very clear that many doctors are unaware of the importance of these as essential documents for travel purposes, if one may judge by the inaccurate way in which they are completed. It is not uncommon to find that, though an international certificate has been asked for, the individual is supplied with a certificate written on the doctor's notepaper, or indeed on a sheet of blank paper. Such a certificate is valueless for travel purposes. It is also essential that the doctor's signature should be authenticated by his local public health authority and duly stamped by that authority.

May I quote a very recent example reported from one of our ships? There were no fewer than 95 invalid certificates issued by doctors in all parts of the country; many of these lacked the official "approved stamp," many were undated, and others failed to indicate whether a primary or a revaccination had been done, and often no result was recorded. Thanks to this, a large number of passengers had to submit to revaccination on board before reaching their destination. You will appreciate how annoying this is for the individuals concerned.

In many countries admission is granted only on production of a valid vaccination certificate, and this is looked upon abroad as a legal document of no less importance from the point of correctness than passengers' other immigration documents. International vaccination certificate forms are obtainable from local public health authorities, from main passenger offices, or from the Ministry of Health.

The correct method of dating is indicated in the "Notes" set out in the certificate.—I am, etc.,

London, E.C.3. I. J. CORBETT,
Medical Superintendent,
Peninsular and Oriental Steam Navigation Company.

Poisoning by Tolbutamide

SIR,—Very few serious toxic side-effects have been observed or described from the use of tolbutamide in the attempted oral treatment of diabetes mellitus, although everyone was watching for the probability on account of the bad reputation of the previous sulphonyl-urea carbutamide. So I think it right to report a serious condition that developed in one of my diabetic patients while the drug was being tried. His stout father had mild diabetes mellitus which ended in gangrene.

He was a sturdy, middle-aged man, who had been referred to me for diabetes discovered during a life assurance examination in 1940 at the age of 43. He had no serious symptoms—occasional slight thirst and polyuria—and there was no need to treat him in any way but a restricted carbohydrate diet. This could clear him of sugar; but I think he rarely followed the diet, and year after year his urine contained traces to 3% of sugar, but there was no ketosis and his blood-sugars varied from 160 to 320 mg. per 100 ml., and were mostly at the latter level. Otherwise he was organically normal—vigorous enough to do his work easily as a builder.

By 1956 I noticed slight opacities in the lens and one or two small haemorrhagic lesions—smudge haemorrhages, and some small aneurysms—and when the sulphonyl-ureas were introduced I contemplated using carbutamide, but put this off until the less toxic form was introduced. I gave this partly on account of his eyes and because he was getting troublesome cramp from time to time as well as his occasional thirst and polyuria. He was still somewhat obese, but his weight had fallen from 14½ stone (92 kg.) to 13½ stone (86 kg.). A few weeks ago he was put on tolbutamide, starting with 1 g. morning and evening, and as the sugar went rapidly down he was given 1 g. in the morning and 0.5 g. in the evening.

I soon received a letter from Dr. J. D. M. Lytle, of Oxshott, asking me to see the man again, saying that after a week the sugar had completely disappeared, the blood-sugar had fallen to 170 mg. per 100 ml., but (and it was a big "but") his liver was enlarged, his belly swollen, he was breathless, and had oedema of the ankles. He had no heart pain and his blood pressure remained unchanged, 150/60. When I saw him all the above was obvious. He was unable to work, felt very ill, being especially troubled with breathlessness and general weakness. The liver, some three fingers below the right costal margin, was smooth and slightly tender and easily enough felt in an abdomen distended with ascitic fluid. He had pitting oedema up to the knee, but there was no change in the slight albuminuria he had had for years, nor in his blood pressure. There was no appearance of jaundice either in the urine or in the eyes. I neglected to estimate the blood bilirubin, and, although I felt this was unimportant, it would have been interesting.

Everything pointed to the enlarged liver as the cause of his troubles, so I stopped his sulphonamide at once, wrote to his doctor about the situation, and advised some mercurial diuretic if the oedema persisted. However, a week's rest in bed without tolbutamide, though perhaps a 250-mg. tablet daily of acetazolamide helped, removed all his previous troubles. The sugar soon came back to its previous level, but general health was good and strong and he was able to work again.

I know well enough that one must be cautious about *post hoc propter hoc*, but I personally have little doubt that sulphonamide was the cause of this serious period of ill health.—I am, etc.,

London, W.1. R. D. LAWRENCE.

Hydroxydione Injection Technique

SIR,—In their paper in the *Journal* of February 7 (p. 332) Drs. Archibald H. Galley and L. H. Lerman make the point of minimizing the time that hydroxydione is in contact with the vein endothelium as a means of reducing the incidence of post-operative thrombosis following use of this drug. Even with very rapid injection they were still finding a very much higher incidence of post-operative thrombosis than with the patient on the commonly used barbiturates.

If rapid transport of the drug from the vein is in fact an important factor we can make a suggestion which may further help to reduce the incidence of thrombosis. It has been shown previously[1] that reactive hyperaemia following the release of an arterial tourniquet decreases the time of onset of intravenous barbiturate anaesthesia presumably by increasing the venous return from the limb. Subsequent unpublished investigations have shown that the optimum effect is obtained 10–15 seconds after the release of the tourniquet following the period of arterial occlusion of 3–5 minutes. This coincides with the flushing of the limb. Measurements of forearm blood flow, using venous occlusion plethysmography, revealed increase of forearm blood

flow of 100–450% lasting for half a minute. This must be accompanied by a considerable transient increase in venous return.

This technique has been used in a small series of cases with a new thiobarbiturate (N-methyl-5-ethyl-5-sec-butyl thiobarbiturate acid) which in 5% solution causes an appreciable incidence of post-operative thrombosis—24% in our series. When the method of injection described above was used this was reduced to 4%, with a further 8% of doubtful cases. Our numbers are too small to be subjected to statistical tests, but the results are highly suggestive.—We are, etc.,

JOHN W. DUNDEE.
LEO. MCARDLE.

Department of Anaesthetics,
Institute of Clinical Science,
Belfast.

REFERENCE

1 Dundee, J. W., *Brit. J. Anaesth.*, 1957, **29**, 440.

SIR,—In the course of their article "New Technique with Hydroxydione" (*Journal*, February 7, p. 332), Dr. Archibald H. Galley and Dr. L. H. Lerman, when discussing post-operative vein thrombosis, state that "thiopentone has a post-anaesthetic thrombosis rate between 17 and 20%, but, being painless, largely goes unnoticed."

In a series of 200 cases using a 5% solution of thiopentone, we found only one case of venous thrombosis (an incidence of 0.5%) in a 48-hour post-operative period.[1] This was in fact painless, but, since we personally examined all these patients, we feel confident that no other cases occurred in this series. We believe, therefore, that, assuming a reasonable technique in venepuncture, the figures given by Drs. Galley and Lerman in this connexion are unnecessarily high.—We are, etc.,

J. M. HALL.
A. M. HUTTON.

Guy's Hospital,
London, S.E.1.

REFERENCE

1 Hutton, A. M., and Hall, J. M., *Anaesthesia*, 1957, **12**, 467.

Mortality from Tobacco

SIR,—I was very much interested in the article by Dr. R. Doll *et al.* (*Journal*, February 7, p. 322), in which the significance of the differences in length of cigarette ends in England and the U.S.A. with regard to the mortality from lung cancer in both countries was discussed.

In the first half of 1958 I made a similar investigation in the Netherlands. Cigarette butts from a restaurant, an office, a railway station, and from canteens for officers and for laboratory personnel were collected and measured after the method of Hammond in the U.S.A.[1]

As in most countries the popularity of filter cigarettes is of very short duration—in 1951 the percentage of filter cigarettes in the U.S.A. was only 0.7%[2]—for studies of lung cancer non-filter cigarettes are the most important. In the Dutch investigation 90% of the butts were from non-filter cigarettes; the English and American percentages were 85% and 40%. In each separate country non-filter and filter cigarettes are smoked to almost the same length, the average length in Holland being 20.5 and 23.3 mm., in England 18.9 and 17.6 mm., and in the U.S.A. 30.7 and 31 mm. Our table shows that the Netherlander and the Englishman smoke their cigarette much nearer to the end than does the American. In this the smoking habits in Holland and England, where in comparison with the U.S.A. the mortality from lung cancer is disproportionately high, do not differ much.

Comparison of Cigarette Ends Measured in the Netherlands, U.S.A., and England and Wales

Length of Butt (mm.)	Non-filter Cigarettes		All Cigarettes (Filter and Non-filter)		
	U.S.A. (%)	Nether-lands (%)	U.S.A. (%)	Nether-lands (%)	England and Wales (%)
Up to 9·5	1·8	2·0	0·8	1·8	1·2
10–14·5		15·2 17·2		13·8 15·6	17·5 18·7
15–19·5	7·6	31·5	7·9	32·4	46·7
20–24·5	17·1	28·8	19·7	28·7	25·4
25–29·5	22·1	13·2	19·9	13·0	6·9
30–34·5	21·8	4·9	20·9	5·3	1·4
35–39·5	12·6 51·6	2·6 9·3	12·8 51·7	2 9 10·3	0·6 2·3
40+	17·2	1·8	18·0	2·1	0·3
Total butts measured	1,697 (100%)	798 (100%)	4,283 (100%)	890 (100%)	772 (100%)
Average length (mm.)	30·7	20·5	30·9	20·8	18·7

As Hammond's technique for collecting the butts differs greatly from the technique which was adopted by Doll *et al.*, this difference in method could have been prejudicial to the comparability of their results. However, the parallelism between the English and the Dutch data is an indication that this is not so, and that the difference between the smoking habits in the U.S.A. and our two European neighbour countries is real. Our conclusion is, therefore, that the Dutch investigation adds new evidence to the suggestion that the habit of throwing away a large unsmoked butt may contribute to the relatively low mortality from cancer of the lung in the U.S.A.—I am, etc.,

Amsterdam. R. KORTEWEG.

REFERENCES

1 Hammond, E. C., *Brit. med. J.*, 1958, **2**, 649.
2 *False and Misleading Advertising. Hearings before a Subcommittee of the Committee on Government Operations, House of Representatives. 85th Congress, First Session. July, 1957.* U.S. Government Printing Office, Washington.

The Influenza Epidemic

SIR,—May I add some comments on the influenza epidemic to those of other G.P.s? (*Journal*, February 21, p. 501). In my practice the interest has been focused on the chest cases. Children have been brought to the surgery with a cough and cold, and on examination it was found the children had a moderate pyrexia with moist sounds in one or both lungs, indicating a patch of pneumonia. Two children were brought with a cold and some abdominal pain, and it was found that these two had a small patch of pneumonia. I have seen an average of three such cases per week up to February 17. They all cleared rapidly with "sigmamycin" syrup, or oxytetracycline.

I wonder whether anyone else has seen chest cases of this nature, which could easily have been missed.—I am, etc.,

Bromley, Kent. J. HUME STEWART.

SIR,—We are told of diseases in search of viruses[1]—parent hosts looking for lost children: doctors also are constantly in search of viruses old and new, known and unknown. To the family doctor, chasing viruses is an occupation akin to entomology: it provides the same interest and satisfaction which come from spotting the first Brimstone butterfly of early spring or the last hibernating Tortoiseshell of autumn.

Influenza was suspected in this practice (*Journal*, February 21, p. 501) during early December of last year

but was not confirmed serologically. Christmas week saw three out of a family of six taken ill simultaneously, and paired sera from one victim proved the infection to be due to influenza virus A. A further sample of blood was taken on the 29th day after onset of illness (January 22) and showed a titre of 1/30 in the haemagglutination-inhibition test, thus confirming that the strain was Asian type A. The same strain was cultured from garglings taken from another patient on January 28.

Influenza of this type occurred sporadically in the practice during the first three weeks of January and seemed to attack only those who had not had Asian influenza in the autumn or winter of 1957. When the disease spread rapidly during the week beginning Monday, January 19, this preliminary impression was amply confirmed and permits the modest conclusion that immunity conferred by an attack of Asian type influenza A lasts not less than fifteen months. The epidemic has flourished for four weeks and has passed its peak of popularity. There has been one death (a man of 79) in a practice of some 3,700 at risk. Attack rate is most difficult to assess, but it is likely to be less than the 15% estimated to have succumbed to the Asian epidemic of 1957 and to the influenza type A1 epidemics of 1951 and 1956.

Meanwhile, by mid-January it was known that influenza B virus was around, causing outbreaks mainly in schools and institutions. On January 31 three children from a nearby school outbreak were found to have an influenzal-like illness, acute in onset but mild in degree, and all three were known to have had Asian type A influenza in 1957. Influenza B infection may be ephemeral, here to-day and gone to-morrow, and, if it attacks children, serological confirmation, nice though it may be for the doctor, is not welcomed by the patients.

Paired sera from a further case of proved influenza A disease also showed a consistently raised titre to influenza C antigen. The patient gives no history of any previous illness sufficient to justify the diagnosis of influenza: indeed, her immunity to influenza C may have been acquired without any illness. Influenza C has not been spotted in this practice before. Garglings (taken on January 21) from another patient produced no virus on culture, but paired sera showed this man to have been infected with Sendai virus. It is easy to be wise after the event, but his illness could have been distinguished from that caused by influenza A: the rapid recovery after 48 hours of sweating and "steaming" and the almost complete absence of both post-influenzal catarrh and debility were noted.

One further impression for comment. The expected overall rise of mortality from all causes[2 3] has occurred here during this epidemic: it was noticeable by its absence here in the autumn of 1957. There is some evidence in support of the hypothesis that influenza contributes directly to most of this accepted excess mortality. The immediate cause of death in the elderly is often cardiac failure, which is easily recognizable; it is not so easy, in the elderly, to recognize an attack of influenza which precedes the cardiac failure. Nor is it often convenient, even if it were possible, to take sera or garglings from such patients. The season of the year in which the epidemic strikes would, however, seem to be an additional factor in this context: we have not much experience of autumnal influenza epidemics in this country. Finally, the layman's diagnosis: "We all had the 'flu last week, doctor," used to arouse scientific scepticism. But more respect will be paid in future to the opinions of those who announced that influenza was in the area a week or so before it was diagnosed by the writer.

Identification of the field samples is part of the excellent work done by the Public Health Laboratory Service. Dr. J. Boycott, of Taunton, and Dr. B. Moore, of Exeter, supply advice and most of the technical information as generously as they provide encouragement.

—I am, etc.,

Clevedon, Somerset. ALASTAIR MACLEOD.

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2 Martin, W. J., *Brit. med. J.*, 1950, **1**, 267.
3 Deutschman, Z., *Influenza, Wld Hlth Org. Monogr. Ser.*, No. 20. Geneva.

Glucose

SIR,—The report of the Food Standards Committee[1] would not at first sight seem to concern us. On the other hand, there appears to be an indirect criticism of the use of oral glucose medicinally in preference to cane sugar.

We are not concerned with the effect of this report on manufacturers of soft drinks. We must, however, be alert to any possible extension of condemnation of glucose or liquid glucose in therapeutics. Only a few years ago we were nearly deprived of heroin on a committee's advice to the Minister concerned, and in fact this battle was won, not on medical opinion, which was ignored, but by the timely intervention of the late Lord Jowitt. This may not be a strict parallel, but it behoves us to watch the situation closely and to protest if developments threaten our therapeutic freedom.—I am, etc.,

London, W.1. A. H. DOUTHWAITE.

REFERENCE

1 Food Standards Committee of the Ministry of Agriculture, Fisheries, and Food. *Report on Soft Drinks*, 1959. H.M.S.O.

Tracheotomy

SIR,—I am sure all who are now dealing with the present influenzal epidemic of severely ill children will agree with the advice and warnings mentioned in your annotation on tracheotomy (*Journal*, February 14, p. 429). They also apply to the adult "smog" casualties. The unsuspected slipping out of the outer tube, the gradual obstruction of the tube by inspissated pus and blood (especially if the inner tube has had the upper curve cut away), and the large crusts in the trachea not sucked out through the tube are certainly three of the many hazards that need constant watching for, day and night. I find help for house-officers and nurses (as well as myself) in having a small, flat piece of cotton-wool to hold over the tube orifice occasionally, to indicate in-flow and out-flow.

An additional warning is suggested by Drs. Ann M. Peach and Elisabeth Zaiman in their article on acute laryngo-tracheobronchitis in children (*Journal*, February 14, p. 416). Preliminary laryngoscopy for suspected epiglottitis or bronchoscopy for suction may be dangerous. It can cause sudden, severe bronchial as well as laryngeal spasm. In a recent experience of mine, a child of 4 months would have died, in spite of urgent tracheotomy, if expert anaesthetic help had not been available.

I should like to add a plea for the occasional use of the laryngotomy operation. Some of these patients are taken very acutely ill so suddenly that an opening below the glottis is urgent. If no surgeon is readily available, a house-officer will more easily be able to save a life by doing a quick transverse stab laryngotomy than by doing a difficult tracheotomy. A tracheotomy is then performed shortly afterwards by a competent surgeon. So long as the laryngotomy tube is not left *in situ* longer

than 12 hours, there is little danger of cricoid perichondritis. The argument about two operations being done is not a serious one.—I am, etc.,

London, W.1. IAN G. ROBIN.

Children with Pneumonia

SIR,—Professor Wilfrid Gaisford, in his article on "Drug Treatment of Infants and Children Suffering from Pneumonia" (*Journal*, January 24, p. 230), gives details of an expectorant mixture which may be prescribed in infants with bronchopneumonia (with presumably copious secretions, as he mentions "copious moist rales").

I wonder whether it was that he felt himself bound by the general title of the series "Drug Treatment of Disease" that he did not mention postural drainage in such infants, or whether he does not use this procedure. In my department we find gravity and gentle percussion over the most affected part of lung the most effective expectorant, and have frequently rendered infants almost suffocating in their own secretions on admission pink and restful following postural drainage and suction of the pharynx. (The secretions thus obtained are then available for culture.) No doubt this procedure is common practice in Professor Gaisford's wards as in many centres, and it will be found efficacious in many other respiratory problems from those in the newborn to those in the asthmatic. In the infant and young child it is so easy for the mother or nurse to put it over her knee or the side of the bed before feeding—for 5 or 10 minutes—each five minutes of efficient postural drainage being in my estimation better than any amount of orally administered expectorant.—I am, etc.,

Paediatric Department, Regional Hospital, Galway. BRIAN MCNICHOLL.

SIR,—I thank Dr. Brian McNicholl for his comments. Although the title of the series inevitably influenced the contents of my article I must confess that, even if the title had been a comprehensive one on treatment *in toto*, I would not have mentioned physiotherapy in considering *acute* pulmonary infection. It is necessary in many cases to nurse an affected infant in an oxygen tent, and, in the more severe infections which impose severe strain on the myocardium, the greatest gentleness and care are required if the infant is to survive. The idea of putting such an infant over the side of the bed "for 5 to 10 minutes before feeding" is, to put it mildly, rather alarming. Dr. McNicholl is, of course, quite right in stressing the value of postural drainage combined with light percussion *after* the acute phase is over, particularly when there are residual areas of collapse in the lung.—I am, etc.,

Department of Child Health, University of Manchester. WILFRID GAISFORD.

Respiratory Failure in Bronchitis

SIR,—The respiratory depression resulting from carbon-dioxide retention not only reduces ventilation but also suppresses the cough reflex. This aggravates the sputum retention which is the primary cause of the emergency. Mechanical suction methods are valuable, especially when applied through a tracheotomy, but they probably remove secretion only from the larger bronchi. In many of these patients it appears that the chief need is to stimulate coughing, the most effective method of clearing smaller bronchi.

When aspirating secretions in comatose patients by means of a long intratracheal catheter, we have noted that contact of the catheter with the carinal region often induces a powerful coughing paroxysm, enabling increased amounts of sputum to be aspirated. In some cases this produces prompt improvement in colour and return of consciousness, and this relatively simple procedure is well worth a trial before tracheotomy is resorted to. If it is thought advisable, the catheter can be used for administration of oxygen after aspiration of sputum.

We have had invaluable help from our anaesthetist colleagues in carrying out these intubations in medical wards.

—We are, etc.,

J. A. S. BRINE.
A. L. JACOBS.

Whittington Hospital, London, N.19.

Domiciliary Physiotherapy Teams

SIR,—In the treatment of those suffering from chronic bronchitis and emphysema, postural drainage and breathing exercises surely play the major part. In most cases, however, it is essential that this form of treatment be carried out at home to avoid travelling, so often in bad weather, to the hospital physiotherapy department.

Often I have found it possible to instruct a member of the patient's household to carry out postural treatment early in the morning, about half an hour after the patient has had an antispasmodic (a strammonium mixture or ephedrine) and a hot cup of tea, with good results. This, however is not always possible. Therefore, I believe that much could be done to relieve patients, the overloading of hospital beds, and the use of expensive antibiotics in having teams of domiciliary physiotherapists and trained volunteers attached to all hospital areas.—I am, etc.,

Stroud, Gloucestershire. G. F. KNIGHT-WEBB.

The Newer Steroids

SIR,—The last paragraph of your annotation on "The Search for New Steroids" (*Journal*, February 14, p. 429) gives me the impression of throwing a good deal of doubt on the advantages of the new steroids. I have already written to you to point out the real advantages of buffered prednisolone for radiation complications (*Journal*, October 26, 1957, p. 1000). Since then experience of the newer steroids—methyl prednisolone and especially dexamethasone (methyl fluoro-prednisolone)—has shown their value, especially of the latter in the absence of side-effects observed. A very severe "moon face" was produced by triamcinolone given by one of my colleagues in the management of a myeloid leukaemia under irradiation.

Recently, two patients—one with "swelling of the face and discomfort around the eyes," and another with "indigestion"—got prompt relief on changing from methyl prednisolone to dexamethasone. It seems that an extended trial of the latter might be indicated.—I am, etc.,

London, W.1. ANTHONY GREEN.

SIR,—In your annotation (*Journal*, February 14, p. 429) "The Search for New Steroids," you state that, "To the clinician using steroids for prolonged treatment, particularly in rheumatoid arthritis, the two main bugbears are peptic ulceration and osteoporosis." While in agreement with this statement it would have

been useful to mention that osteoporosis may be at least alleviated by treatment, and I would like to briefly mention the following illustrative case.

A boy had an attack of polyarthritis diagnosed as rheumatic fever in 1953 when aged 12. In 1955 he was readmitted to hospital with very high fever, mild polyarthritis, and pericarditis, with an extremely high leucocyte count. The diagnosis of Still's disease became obvious. He was treated with corticotrophin and then with prednisolone. It was found impossible to discontinue treatment with steroids, as, on diminishing the dose to less than 20 mg. of prednisolone per day, fever and malaise promptly recurred. He developed gross evidence of hyperadrenalism, with moon-face, red striae, and wasted flabby muscles.

In February, 1958, he was readmitted with severe backache. *X*-rays showed gross generalized osteoporosis with multiple compression fractures of vertebral bodies. The serum calcium was 10.8 mg., and 24-hour urinary calcium excretion was 0.67 g. on an average diet. The patient was seen by Professor C. E. Dent, who advised treatment with methyltestosterone, 10 mg. thrice daily. Slowly bone pain disappeared and the patient could be mobilized. Urinary calcium values fell to 0.1–0.3 g. per day.

In May, 1958, jaundice appeared with the typical biochemical findings of intracanalicular obstruction, and this was thought to be due to the toxic effect of methyltestosterone. Since then the patient has been treated by a weekly injection of 25 mg. of 19-norandrostenolone phenylpropionate ("durabolin"). The bone pain has not recurred and urinary calcium values average 0.1–0.14 g. per day. The patient has continued on treatment with triamcinolone in a dose of between 12–16 mg. per day to date.

It would thus seem that, when patients require continued treatment with steroids in high dosage, it is worth while to add a weekly injection of durabolin or another similar preparation.—I am, etc.,

Whittington Hospital,
London, N.19.

E. MONTUSCHI.

Herpes Zoster during Steroid Therapy

SIR,—Herpes zoster, often causing severe pain and sometimes resulting in disablement, has attracted many empirical methods of treatment. The search for a remedy continues, and in more recent years the use of cortisone or corticotrophin has been suggested. Duke-Elder[1] reported improvement in four cases of zoster iridocyclitis treated with cortisone. Since then a number of favourable reports on such treatment have appeared. Carter and Royds,[2] referring to these reports, were more guarded in their conclusions regarding their own results with prednisone and antibiotic treatment in 15 cases of ophthalmic zoster, but found that oedema was less, drying of the rash quicker, and scarring much less than in a control group. The disease, however, is so variable in its symptomatology and sequelae that until a controlled trial is carried out on a larger scale some doubt must remain regarding the real value of such treatment. On the other hand, since herpes zoster is a common disease and since cortisone-like and corticotrophic drugs are now widely used in the treatment of many unrelated diseases, it may be possible to assess whether such steroids have any effect in herpes zoster by noting the occurrence and severity of zoster if it should appear during steroid treatment of other diseases. Such considerations prompt us to report the following case in which it would appear that corticotrophin did not suppress the onset or ameliorate the progress of herpes zoster, which occurred during maintenance treatment of a case of mycosis fungoides.

A man aged 54 years who suffers from an exfoliative erythroderma (histologically premycosis fungoides) of two years' duration is well controlled by intramuscular corticotrophin. Treatment with corticotrophin was commenced on June 11, 1956, and 30 i.u. corticotrophin gel daily intramuscularly continued until March 3, 1958, when the dose was increased to 40 i.u. gel daily. During this period there were no side-effects and the serum chemistry remained within normal limits.

On March 22, 1958, the patient developed herpes zoster on the left side of the thorax, posteriorly, in the axilla, and on the upper abdomen. The onset was accompanied by a mild pyrexia of 99–100° F. (37.2–37.8° C.), which was maintained for two days. Pain was fairly severe but was relieved by codeine. The lesions spread and formed an almost continuous band round the left side of chest and upper abdomen in the distributions of T.6, 7, and 8 (see Fig.).

At this time several discrete vesicles were found on the arms, thighs, and legs. Investigations carried out were: Hb 13.3 g./100 ml.; W.B.C. 9,600/c.mm.; chest radiograph showed bronchitic changes and emphysema but no other abnormality; radiograph of thoracic vertebrae showed no abnormality; serum chemistry was normal.

One week after the onset the lesions in the axilla ruptured, became crusted, and in a few days progressed to superficial ulceration. By April 1, 1958, the main eruption became ulcerated and eventually healed with scarring about six weeks after the onset. The patient now shows numerous white areas of scarring in the distribution of the original lesions.

Although malignancy or blood dyscrasia cannot be completely excluded as aetiological factors in this case of herpes zoster, no evidence of either was found, and we consider that the virus infection was unrelated to the existing condition of mycosis fungoides. No matter what precipitated the onset of the eruption, corticotrophin in a dosage of 40 i.u. gel daily for 20 days previously did not prevent its appearance; nor was the progress of the disease altered by maintaining this dosage throughout its course, for the eruption which was associated with severe pain was in no way abortive and proceeded to superficial ulceration and scarring. On the other hand, no aggravation of the virus infection took

place and neurological and cerebral complications did not occur. The sparse, discrete vesicular lesions on parts remote from the main site of the eruption cannot be taken as evidence of exacerbation towards herpes zoster generalisata, since such lesions are to be found in almost all cases of zoster if careful search for them is made.

No general conclusion can be drawn from this single case, but McNicol[3] has described the Ramsay Hunt syndrome occurring in a patient who was receiving cortisone for ulcerative colitis, and further negative evidence of this nature would be valuable in any future attempt to assess the place of cortisone and allied drugs in the treatment of herpes zoster.

We wish to thank Dr. W. Ferguson Anderson and Dr. A. Girdwood Fergusson for permission to publish this note, and we are indebted to Dr. Thomson for providing the photograph.

—We are, etc.,

Foresthall Hospital, Glasgow. J. S. CREIGHTON.
Stobhill General Hospital, Glasgow. W. A. DEWAR.

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2 Carter, A. Barham, and Royds, J. E., *Brit. med. J.*, 1957, **2**, 746.
3 McNicol, G. P., *Scot. med. J.*, 1958, **3**, 93.

Corticosteroids in Ulcerative Colitis

SIR,—We were extremely interested in the article by Dr. S. C. Truelove and Professor L. J. Witts (*Journal*, February 14, p. 387), because we also have had an opportunity of comparing cortisone and corticotrophin in severe rheumatoid arthritis and have found that in some respects corticotrophin is superior.

Another advantage not considered in the above trial is that with corticotrophin the level of adrenal stimulation produced can be measured by estimating the urinary steroid excretion. We have been doing this for the last four years on both in- and out-patients, using Norymberski's methods of measuring the 17-hydroxy-corticosteroids. Through this method of biochemical control we have been able to watch the level of adrenal stimulation. We have shown[1] that in rheumatoid arthritis a satisfactory suppression can be achieved with much smaller doses than used in the trial by Dr. Truelove and Professor Witts, and that hypercortisonism can be avoided by reducing the dose when the urine tests show that adrenal stimulation becomes excessive. In their excellent trial it should have been possible to lower the high rate of complication with corticotrophin by adjusting the dose according to the level of adrenal stimulation.—I am, etc.,

The West London Hospital Medical School, London, W.6. O. SAVAGE.

REFERENCE

1 Savage, O., Chapman, L., Robertson, J. D., Davis, P., Popert, A. J., and Copeman, W. S. C., *Brit. med. J.*, 1957, **2**, 1257.

Twin Pregnancy in Double Uterus

SIR,—The case reported by Dr. N. Kennedy (*Journal*, February 21, p. 486) of simultaneous pregnancy in each horn of a completely double uterus is of considerable aetiological significance, especially if studied alongside the one to which he makes reference.[1] In this latter, there was a history of two successful and normal previous pregnancies, single ones, of which the second clearly occurred in the right horn—quite possibly the larger of the two—of a completely double uterus. The third pregnancy resulted in twins. One twin occupying this previously distended right horn was delivered at 32 weeks, at which time there was no evidence of toxaemia. The second twin, occupying the left and presumably virgin horn, gave rise to a state of pre-eclampsia. In a very meticulous clinical report there was no mention of placental abnormality. Presumably in this instance the resistance to stretch of the primigravid left horn provoked the toxaemic change without placental intrusion into the aetiology.

In Dr. Kennedy's case the first two pregnancies were successful, and apparently normal, whilst the next two resulted in abortions. The fifth pregnancy was a twin, occupying each horn of a completely double uterus. Here again indirect evidence indicates that the toxaemia which ensued with the first twin was attributable to the primigravidity and the lesser size of the horn in which it was implanted—the right one—since the *x*-rays revealed it to be the smaller of the two. Once the distension factor was overcome by delivery of the conception from this half, toxaemia abated completely. Thus as in the previous case the factor of resistance to stretch by the myometrium becomes revealed as aetiologically responsible for the pre-eclampsia. Since the foetus associated with the toxaemia had a swallowing defect, hydramnios could well have been in association, augmenting the myometrial resistance to stretch and thereby enhancing the aetiological stimulus.[2] The oedema of hands and feet of the foetus associated with the toxaemia is difficult to explain, as foetal oedema never occurs as a consequence of pre-eclampsia.[3] The placenta has no primary aetiological responsibility for toxaemia[2]—a fact undenied by a critical evaluation of Dr. Kennedy's data.—I am, etc.,

London, W.1. JOHN SOPHIAN.

REFERENCES

1 Williams, B., and Cummings, G., *J. Obstet. Gynaec. Brit. Emp.*, 1953, **60**, 319.
2 Sophian, J., *Lancet*, 1959, **1**, 310.
3 McCance, R. A., 1958, personal communication.

Atony of the Female Bladder

SIR,—May I reply to the letter by Mr. J. P. Mitchell (*Journal*, February 7, p. 365) following my paper on "Atony of the Female Bladder" (*Journal*, January 17, p. 149)?

I agree that each of the four cases I described was clinically a case of chronic urinary retention, but I think the paper made it quite clear that the cause was in the bladder wall and not due to obstruction lower down. Mr. Mitchell's suggestion that the absence of hydronephrosis and hydro-ureter in these cases is due to the bladder wall taking the full load of the back pressure does not seem acceptable. If this were so why is the phenomenon not seen more frequently in the chronic retention due to prostatic enlargement, which is invariably associated with some degree of upper renal tract dilatation? The normal blood urea has also to be accounted for.

Although the lower half of the bladder in my first case was not examined histologically, no ganglion cells were found in any sections of the bladder removed by partial cystectomy. A more characteristic feature of the histology of these cases is, however, the fibrous-tissue formation around the muscle bundles. This is not seen to my knowledge if the bladder wall is examined in any form of obstructive lesion. My one-line description of the bladder neck in Case 1 was sufficient, I think, to show that from the bladder aspect it appeared and felt normal. It later proved to be histologically normal also. It was part of the cysto-urethroscopic examination in each case to palpate the bladder neck over the instrument per vaginam, and in each case it felt normal. The absence of any urinary symptoms in the history is also against a bladder neck lesion.

Mention is made on several occasions in the paper of the smooth folds of mucous membrane seen on cystoscopy. It is this appearance and the absence of any trabeculation at all that distinguish the condition from an obstructive bladder. This appearance of enormous smooth folds of bladder wall is, we feel, the most important way of diagnosing the condition. Partial cystectomy is a procedure that on mechanical grounds should improve the condition; and, although, as I pointed out, the residual urine may increase after operation, it is unlikely the bladder will dilate enormously again. One would expect the atony and fibrous-tissue formation in the bladder wall to be self-limiting.

Surely the absence of trabeculation of the bladder wall, the absence of distension of kidney, pelvis, and ureters, the normal blood urea, the absence of obstructive urinary symptoms, the normal appearance of the bladder neck, and the typical histology of the resected bladder wall in these cases point to the condition being one of primary atony. A similar condition is not infrequently seen in the colon where atony occurs in later life, and at laparotomy for symptoms of chronic intestinal obstruction no organic obstructing lesion is found.—I am, etc.,

North Staffordshire Royal Infirmary, Stoke-on-Trent. H. S. TRAFFORD.

Unilateral Amblyopia

SIR,—Although Mr. R. B. Wellesley Cole (*Journal*, January 24, p. 202) is to be congratulated on drawing the attention of the medical profession to the importance of diagnosing and treating unilateral "suppression amblyopia" at the earliest possible age, I think he should have mentioned that: (*a*) some degree of amblyopia may be present in a patient with normal binocular single vision. Such amblyopia is usually associated with anisometropia and may gradually lessen if corrective spectacles are worn constantly (often without any occlusion); (*b*) slight amblyopia for distance vision may be associated with normal near vision; and (*c*) an apparently "useless" (or "grossly defective") eye with regard to *visual acuity* may be of great value from the point of view of *visual field*.

I would agree with Mr. Wellesley Cole that amblyopia should be tackled in earliest infancy, although I think many people will find it difficult (in the absence of strabismus) to believe that "it is possible to diagnose amblyopia even in the youngest baby." Certain signs, however, may lead one to suspect an amblyopic eye in an infant, especially if there is a positive family history.

I should like to know what Mr. Wellesley Cole means by his statement that "a baby is wall-eyed." Such a colloquialism is likely to be misleading, and one can only assume that he means to imply what Chavasse did by stating that "all infants are born with bilateral amblyopia" and that the development of the function of the fovea is largely a matter of the development of a conditional reflex.

Few ophthalmologists will agree that refraction in a child is better done without a cycloplegic, although careful preliminary examination before prescribing atropine is most important. Although it may be difficult to insist that a routine ophthalmic examination should be made when a child is, say, 2 or 3 years old, in order that the early diagnosis of amblyopia and strabismus can be made and their treatment undertaken, yet it is surely not too much to hope that all infants born of squinting or amblyopic parents, or in whose families such conditions are known to exist, should be so examined. If this were done and early treatment instituted the percentage of persons with amblyopic eyes would, I think, be substantially reduced.

Finally, Mr. Wellesley Cole has omitted to mention the valuable work of Cüppers in connexion with the after-image method of treatment, especially in cases of eccentric fixation. By this method many cases of severe amblyopia have been considerably improved at the age of 6 to 8 years.—I am, etc.,

London, W.1. T. KEITH LYLE.

Surgical Rehabilitation of Delinquents

SIR,—My appreciation of the very interesting and modestly stated paper by Dr. D. A. Ogden (*Journal*, February 14, p. 432) was marred only by one vital omission. He reports that 30 (54.5%) of 55 treated cases were free of reconviction in the two years after their release, whereas the corresponding figure for untreated cases was 34.5%. Unfortunately he does not inform us *how many* untreated cases there were, so that the significance of the difference in these percentages cannot be assessed. It would add greatly to the value of his paper if this one item of information could be given.—I am, etc.,

London, S.E.5. G. M. CARSTAIRS.

SIR,—The article by Dr. D. A. Ogden (*Journal*, February 14, p. 432) was both interesting and stimulating, but perhaps some comment should be made before any conclusions be drawn. As a statement of clinical impression the article is beyond cavil, but as a piece of valuable research it cannot be considered satisfactory as presented and, probably, therefore, not of methodologically sound construction. I would note one or two points.

Firstly, Dr. Ogden invites us to compare quite different groups; differing at least in the presence of some remedial physical disability. One would like to know how the two groups compared from a psychiatric, a social, and a criminological standpoint. For example, a young criminal who has a squint that has become a focus "of resentment" is more likely to be diagnosed as having an anxiety or neurotic state rather than as a psychopathic personality. This latter nosological category, with a generally accepted poor immediate prognosis, might well have been over-represented in the group not in receipt of surgical treatment.

Secondly, even if the two groups were matched the results of the investigation remain suspect in that, apart from the remedial surgery performed, the investigated group were in receipt of considerable additional attention—not inappropriately termed supportive or non-specific psychotherapy. Surely Dr. Ogden has become involved with a number of variables that are now inextricably confused in his research.

A piece of work that is methodologically acceptable, that takes into account all the important variables, is not easy to set up, particularly in a busy Borstal institution. Nevertheless, it is of importance that profound conclusions are not drawn from inadequate work that lacks the necessary degree of methodological sophistication: conclusions such as "it (remedial surgery) renders the individual susceptible to the normal character training processes." I would emphasize that these criticisms are not motivated by any hostile attitude toward the conclusion drawn by Dr. Ogden, on the contrary I would endorse them from my own clinical impression and find them in accord with

experience regarding plastic surgery expressed in the *Sunday Times* of December 8 by Sir Harold Gillies.

My objection to the article is that it is setting out clinical impressions in the guise of research work, the conclusions that are drawn being of very considerable importance. One has only to realize the frequency of minor (not to mention major) physical disability in the delinquent and criminal populations to appreciate the importance of this work, if it can be clearly shown that the conclusions are a true and proper interpretation of the results. If the thesis set out by Dr. Ogden has even a mite of truth in it, then it makes a marked contribution to remedial and prophylactic measures at the command of those concerned with crime and its prevention and cure, but on balance I feel that the problem remains, and will remain, until a more adequately constructed piece of research provides the answer.—I am, etc.,

Thornton Heath, Surrey. ALLEN A. BARTHOLOMEW.

Psychotherapy in General Practice

SIR,—The technique of psychotherapy employed in general practice is less important than diagnosis and familiarity with the natural history of the psycho-neurosis or psychosis involved. Analytical or reconstructive therapy should only be used by those few who are able to undertake considerable technical training; while supportive therapy and some insight therapy (which involve counselling, re-education, and strengthening or reorganization of the ego-defences by various techniques) are the methods employed almost exclusively both in general practice and psychiatric clinics. Their success depends on the one hand upon accurate diagnosis and observation of the progress of the illness, and on the other upon empathy, aptitude, technical knowledge, and mature judgment.

Dr. C. A. Fox (*Journal*, January 3, p. 51) and Dr. M. B. Clyne (*Journal*, February 14, p. 441) suggest and discuss training for a diploma in psychotherapy for general practitioners. The implications of the new Mental Health Bill certainly suggest an increase in domiciliary care of mental illness which might open a wide field to interested and qualified doctors, quite apart from the management of the many cases treated from day to day in practice. But since psychotherapy is only one aspect of the management of any mental patient, any syllabus proposed must involve full basic training in psychiatry even if the emphasis is upon the treatment of the neuroses.

Finally, I would say that in the meantime the increasing co-operation between mental hospitals and G.P.s in the provinces can provide most stimulating contacts; and that I understand that discussion groups of interested doctors with a psychiatrist or psycho-therapist present have been organized with much success. The whole subject merits full discussion, since supportive psychotherapy is the corner-stone of general practice.—I am, etc.,

Brockenhurst, Hampshire. E. B. MCDOWALL.

Inorganic Arsenic

SIR,—In his letter in the *Journal* of December 27, 1958 (p. 1593), Professor A. V. Neale raises the question: "Is there any evidence, in fact, of even the slightest value in inorganic arsenic medication?" My reply to this question is an emphatic "Yes."

Inorganic arsenic, in the form of Fowler's solution, is the *only dependable* remedy for lichen planus, a distressing skin condition which, at least here, seems to be getting more common among all races. It has, of course, to be given judiciously, and should be discontinued at the slightest sign of intolerance; but, if these precautions are observed, it is a safe and successful remedy which at least one dermatologist would not like to do without. To me it seems that organic arsenic compounds are much more dangerous. I have seen several cases of fatal dermatitis after neoarsphenamine and similar preparations, but in thirty years of fairly extensive practice as a dermatologist I have never had occasion to see an arsenical dermatosis or a cutaneous cancer due to metallic arsenic. These cases may occur, but my impression is that they are extremely rare; of 240 patients suffering from cutaneous cancer treated by me, not one gave a history of previous prolonged arsenic medication.

Inorganic arsenic has also been recommended as a remedy for psoriasis; but there I feel its use can be dispensed with.—I am, etc.,

Nairobi, Kenya. FRANK PIERS.

Immunization Programmes

SIR,—Dr. J. S. G. Burnett (*Journal*, February 14, p. 436) has misread my letter (*Journal*, January 31, p. 303) in regard to a point of very great importance. I did *not* imply that there was any doubt as to the response to pertussis vaccine if it were begun very early—namely, at 1 month. What I did say was that there was a probability of sub-optimal response to diphtheria prophylactic if it were to be begun as early as 1 month.

There is a fundamental difference between these two immunities. That to diphtheria is primarily an *antitoxic* immunity; maternal antitoxin passes the placental barrier and persists in the infant's blood for some time, certainly for long enough in a high proportion of infants to modify the effect of diphtheria prophylactic if this is started as early as 1 month. Immunity to pertussis, on the other hand, is an *antibacterial* immunity, and there is no reason to believe that the response to pertussis vaccine in the young baby is affected in this way. The age incidences of the worst effects of the two diseases (which also affect the needs of the case profoundly) are fully in accordance with the difference between the two types of immunity and with the resulting difference in the immunological condition of the young infant in regard to each disease.

It is of course true that not all infants come to us early enough in this respect. But this should not prevent every effort being made (and such efforts can be very successful) to give as many babies as possible the best immunization programme.—I am, etc.,

Reading. E. C. H. HUDDY.

Childbirth without Medical Supervision

SIR,—May I refer to your medico-legal note, "Childbirth without Medical Supervision" (*Journal*, February 7, p. 375), which records that on January 15 Owen Wynne Roberts pleaded guilty before the Bury St. Edmunds justices to attending his wife at her confinement without medical supervision and not in an emergency, "which is an offence against Section 9 of the Midwives Act, 1951"? While not advocating the delivery of babies by husbands, I nevertheless protest against a law which makes this a criminal offence; it may be foolish, but it should not, in my opinion, be a criminal offence.—I am, etc.,

Tetbury, Gloucestershire. JOHN N. H. ANDREWS.

Obituary

W. J. STUART, C.B.E., M.B., F.R.C.S.Ed.

Mr. W. J. Stuart, honorary consultant surgeon to the Royal Infirmary of Edinburgh and the Church of Scotland Deaconess Hospital in the same city, and a past-president of the Royal College of Surgeons of Edinburgh, died in Edinburgh on February 23 in his 86th year after a short illness.

William James Stuart, a son of the manse, was born in Edinburgh on December 17, 1873. He was educated at the Edinburgh Academy and while there created a record by being dux of his class in each successive year, and finished by winning the gold medal for the dux of the whole school. At the University of Edinburgh he graduated M.A. before going on to medicine, and he graduated M.B., Ch.B. with honours in 1899. After holding posts as resident house-physician and house-surgeon in the Royal Infirmary at Edinburgh he became a Fellow of the Royal College of Surgeons of Edinburgh in 1903. In 1906 he was elected honorary assistant surgeon to the Church of Scotland Deaconess Hospital, Edinburgh, and in the following year he was appointed to a similar post in the Royal Infirmary. His work as a surgeon was interrupted in 1914 by the outbreak of the first world war, when he was mobilized as a Territorial officer in the R.A.M.C. and served until the end of 1918 in Great Britain and overseas with the British Forces in Salonika, reaching the rank of major. Thereafter he resumed his surgical practice in Edinburgh, and in 1923 he was elected surgeon-in-ordinary to the Royal Infirmary, holding this position until his retirement in 1938. During the second world war he resumed the charge of surgical wards in the Royal Infirmary for about three years, and also in the Deaconess Hospital. In 1938 he was elected President of the Royal College of Surgeons of Edinburgh.

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These bare facts, however, tell but little of the man and might well be written of any successful surgeon of his day. W. J. Stuart was a very much greater man than merely a successful surgeon. The fact that the same kindly nickname stuck to him from his schooldays till his death will give some indication of his character and how he was regarded by all with whom he came in contact. "Pussy" was so-called for his gentleness and kindness, and he rejoiced in his nickname. For a few months in the Army, when serving in a medical unit where he was the only Edinburgh graduate, he was known as "Uncle," but on the arrival in the unit of an Edinburgh graduate, as he himself loved to put it, "The cat was out of the bag."

As a surgeon he was sound rather than brilliant, but where he excelled was in his handling of his patients. He had the faculty of putting them at their ease and making them his friends whatever their walk in life. They were human beings, not just "cases," and he had little difficulty in winning their complete confidence and even their affection. As a teacher he quickly impressed his students by his utter devotion to his work and patients and by his patent sincerity. His residents found in him a chief by whose example they learned far more than the art of surgery, for in him they had a model on which they could profitably shape their whole lives. His colleagues found a friend, ever ready to help, who was never known to say a bitter word and who could always find the good in everyone.

After his retirement from active practice he never found time hang heavy on his hands, since he had many other interests. He was constant in his attendance at the meetings of the Edinburgh Medico-Chirurgical Society up till a month or so before his death, and was president of the society in 1944. For several years before his death he was one of the presidents of the Samaritan Society of the Royal Infirmary. He played a large and active part in the Scottish National Blood Transfusion Association and was chairman of its executive committee for several years. In recognition of this and other public services he was appointed C.B.E. in 1952. Although retired from practice he continued to keep in touch with modern developments in surgery to the end of his life, and even during his final illness spoke to a medical visitor about the articles in the current *British Medical Journal* and the *Lancet*, and also inquired how the arrangements were progressing for the Joint Annual Meeting with the Canadians in July.

His well-known erect figure will be missed from the streets of Edinburgh. Never caring to own a motor-car, he went about his practice on a pedal bicycle, and after his retirement took his regular exercise by walking. In his younger days he was a keen athlete, and it will surprise many who only knew this quiet, gentle man in his later years to learn that on the rugby field he had been an extremely robust Edinburgh Academical forward, and only missed an international cap by very little, being reserve forward for Scotland in 1901. He was also an accomplished cricketer in his school first eleven, and latterly played regularly for the infirmary chiefs against the residents almost until he retired. In his later days his recreations were fishing and shooting.

Besides his professional and semi-professional interests he took an active part in the work of the church into which he had been born and in which he worshipped regularly throughout his life. With this very real spiritual background he was able to achieve a serenity that was obvious to all. He was blessed throughout his life with good health and found his greatest happiness in his work, whether professional or in the many good causes in which he was interested, and he passed away, full of years, after only a fortnight's illness in the hospital he loved and served so faithfully.

"Nothing is here for tears . . .
. . . nothing but good and fair."

R. T. T.

JEAN LHERMITTE, M.D.

Professor Jean Lhermitte, the renowned French neuropsychiatrist, died on January 24.

Jacques Jean Lhermitte was born on January 20, 1877, at Mont-Saint-Père, Aisne, the son of an artist. His early education was at St. Etienne, and he went on to Paris to study medicine, graduating in 1907. Specializing immediately in neurology, he held clinical and pathological appointments in the Faculty of Medicine in Paris, and at the time of his death he was an honorary professor of the faculty. After the first world war, during which he made a special study of wounds of the spinal cord, he extended his researches into the neuropsychiatric field, and the distinction of his style and intellect marked the many books and papers which he wrote. Autoscopy, or visual hallucination of the self, was one of the subjects he was always interested in, and a paper of his on this topic was published in this *Journal* some years ago. Among the hospital appointments held by Professor Lhermitte was a clinical directorship at La Salpêtrière, the famous hospital for nervous diseases in Paris.

We are indebted to Dr. MACDONALD CRITCHLEY for the following appreciation: On January 24 of this year, Professor Jean Lhermitte, of Paris, died peacefully in his

sleep in his 81st year. In this way there has passed one of the really outstanding figures of medicine. Lhermitte had had in the finest sense of the word an unusually full life. His boyish and captivating enthusiasm drove him incessantly and tirelessly onward, and he never ceased to evince deep interest in contemporary events. Lhermitte was one of the greatest clinical neurologists of all time. His truly brilliant gifts were erected upon a very firm foundation in normal and morbid anatomy of the nervous system. Later there came a keen and searching evaluation of disorders of the mind. He was the *beau idéal* of a neuro-psychiatrist, as shown by his numerous contributions to the literature. Indeed, Lhermitte would not recognize any frontier separating organic neurology and psychiatry. His original studies covered a wide range of interests, embracing neurogeriatrics, disorders of perception, the problem of pain, sleep, corporeal awareness or *l'image de soi*, and highest level visual disorders. He was also a devout churchman and was intrigued by the common territory between theology and medicine. This interest led to his fascinating studies upon such topics as demoniacal possession, and also stigmatization. He was a leading contributor to the *Études Carmélitiennes* as shown by his monograph, upon *Satan* and *Le Cœur*. The last-named subject was treated from the historical angle of the traditional correlation of the heart with the seat of the emotions.

Among Lhermitte's earlier and more strictly neurological studies, we recall his monograph upon the paraplegias of the aged, olivo-rubro-cerebellar atrophy, peduncular hallucinosis, and the barber's-chair phenomenon in cases of disseminated sclerosis. These were merely a few among a veritable galaxy of other contributions.

Lhermitte had an abounding vivacity and until his latter years a vigorous and robust constitution. He seemed never to rest, and he combined a huge practice with continued interest in professional writing. He was a fluent and eloquent speaker, possessed of a truly Gallic *élan*. Neurologists in this country will long remember him as the most sincere and generous of friends, warm-hearted and tolerant, stimulating and encouraging. He gloried in the company of his younger colleagues, to whom he was a mentor and an inspiration.

A. G. PHEAR, C.B., M.D., F.R.C.P.

Dr. A. G. Phear, consulting physician to the Royal Free Hospital, died at that hospital on February 26, aged 91.

Arthur George Phear was born at Croydon on March 16, 1867. From Charterhouse he went on to Trinity College, Cambridge, where he took first-class honours in the Natural Sciences Tripos. Completing his clinical training at University College Hospital, he graduated M.B., B.Ch. in 1891, took the M.R.C.P. in 1893, proceeded to the M.D. in 1895, and was elected F.R.C.P. in 1902.

Elected to the staff of the Royal Free Hospital in 1898, he had been for a short time before that assistant physician at the Metropolitan Hospital. During his long career he was on the staff of several other hospitals, including the Royal Chest Hospital, the Royal National Hospital for Diseases of the Chest, Ventnor, and the Queen Alexandra's Military Hospital, Millbank. During the first world war he was consulting physician to the British Salonika Force and Army of the Black Sea, serving with the rank of colonel, and in 1920 he described before the Royal Society of Medicine his experiences in Macedonia and the Caucasus. Twice mentioned in dispatches, he was appointed C.B. in 1919.

At the Royal College of Physicians Dr. Phear was an examiner in medicine and for two years a member of the council. He also examined for Cambridge University. For ten years he was chairman of the medical committee at the Royal Free Hospital, from the active staff of which he retired in 1928, though he continued to practise as a consultant physician for some time thereafter.

A gifted musician, Dr. Phear was an organist and pianist of distinction. It was characteristic of his kindness and enthusiasm that he should have spent so much of his time directing the Choral Society at the Royal Free Hospital. He often deputized for the organist at All Saints Church, Margaret Street.

Dr. Phear married Ellen Frances, daughter of Arthur Lister, F.R.S., a younger brother of Lord Lister.

F. P. L. L. writes: Arthur G. Phear represented a generation of physicians in whom great culture and wide tastes were as prominent as clinical ability. A reader of English and Greek literature, a wide knowledge of plants and trees, a musician of great talent—all this made up a complex character which to the casual observer was that of a mild man of easy judgments. The kindness of Dr. Phear's heart was there for all to see. His benefactions to the nursing staff of the Royal Free Hospital, who looked after him so ably and well in his long last illness, were marked by the care and thought given to each gift in turn: a piano for the nurses' home, an organ for the chapel, a fund to help nurses to a more comfortable convalescence after illness—these are but a few examples of this trait. He had, however, a quick wit, which, though seldom biting, occasionally stung. His kindness of heart always made him regret remarks made under the stimulus of this wit, and he would try to make up in some other way for what he felt was the unkindness done.

Dr. Phear showed great interest in the affairs of the Royal College of Physicians, and was a councillor just before his retirement from consulting practice. His interest, however, lasted to the end of his life, and from a surprisingly young viewpoint he would discuss the projected move of the College. After his retirement there is no doubt that music was the great love of his life. He was fortunate in that his talent for playing the piano was so great that he did not have to rely on records and the wireless to supply him with the music he loved.

During the first world war he served with great distinction in Macedonia. From there he sent home to his wife weekly typewritten letters of his life. These letters contain descriptions of all the famous places he visited, as well as brilliant thumbnail sketches of the people he worked with. Many of these became famous in medicine later. His descriptions of dust storms and the beauties of the mountain-side are vivid and real, and worthy of the pen of Cecil Roberts.

To the very end Dr. Phear retained his clarity of mind and good memory. To talk and discuss affairs with him was like talking to a man of half his years. His resilience was tremendous, and his recovery from a stroke about eight months ago was litt'e short of miraculous. He was practising medicine before the majority of physicians active to-day were born, and had retired from medicine before many of them had qualified.

T. PEARSE WILLIAMS, M.D., F.R.C.P.

Dr. T. Pearse Williams, physician to Paddington Green Children's Hosp'tal and to Willesden General Hospital, died at the latter hospital on February 22. He was 65 years of age.

Thomas Pearse Williams was born on May 19, 1893, at Plymouth, where his father, Dr. Thomas Henry Williams, was a general practitioner. Educated at Plymouth College, he received his clinical training at the Middlesex Hospital, where, it is interesting to note, both father and son were Broderip scholars, the former in 1885 and the latter in 1916. After graduating M.B., B.S. in 1916, Pearse Williams joined the R.A.M.C. and went to India, spending most of the

remaining years of the first world war at the Deccan British War Hospital at Poona. He was demobilized with the rank of captain in the Special Reserve, and in July, 1919, was appointed the first post-war medical registrar at St. Mary's Hospital. At the end of his year of office he was reappointed for a second year, but resigned a few months later to take up the appointment of medical registrar and tuberculosis officer to the Middlesex Hospital. In 1920 he proceeded to the M.D. and became a Member of the Royal College of Physicians of London, being elected a Fellow of the College in 1937.

His first consultant appointment was that of physician to out-patients at Paddington Green Children's Hospital in 1921. He was elected to the full staff in 1927, having been elected physician to Willesden General Hospital in the previous year. He was made honorary consulting physician to both hospitals on his retirement in June, 1958. During the second world war he did fine work as a physician in the Emergency Medical Service to the Willesden General Hospital. He was a member of the Willesden Division of the British Medical Association, being chairman from 1940 to 1946, and vice-chairman of the Middlesex area committee of the British Hospitals Association from 1946–8. From 1955–8 he was a member of the executive committee of the British Paediatric Association, of which he had been a member since 1936. A member of the executive committee of the Willesden General Hospital for eighteen years, he was chairman of the committee from 1941 to 1948, a special distinction for a medical man. After the nationalization of the hospital in 1948 he served for six years on the Central Middlesex Group Hospital Management Committee. He helped to found the Willesden General Hospital Medical Society, and was the first president. The society presented him with his portrait in oils by David Craig when he retired. Appointed medical officer to the Polytechnic in January, 1924, he undertook a great amount of work there among the pupils and staff until he retired in 1950. His work at the Polytechnic was one of the great pleasures of his life, and even during the last war he found time to make periodic visits to the two junior schools, the pupils of which had been evacuated to the West Country. As a token of affection and esteem, the institution and its friends presented him with a cheque on his retirement.

Dr. Pearse Williams's first wife died in 1949 after a long period of invalidism, during which he nursed her with extraordinary devotion. There was one child by the first marriage, a boy who died at the age of 7 years. His second wife survives him.

F. W. M. P. writes: Pearse Williams was a general physician of the old-fashioned type now becoming extinct. He was a superb clinician, not only concerning the cases of children but also those of adults and the old. I think, however, that he really liked dealing with infants and young people best of all. Always slightly distrustful of some of the modern methods of investigation and biochemistry, he himself relied chiefly on his eyes, his ears, and his hands. He told me recently that he realized his limitations in modern medicine but that he was never too proud or hidebound to ask the advice of his registrar or even of his houseman when he felt his knowledge was lacking. He was ever kind, helpful, and courteous to his patients, and indeed to all around him. His hospital patients were his prime interest in life, as also were his hospitals, and this may be one reason why he was not a prolific writer. I am sure that the financial side of his professional life was a matter of supreme unimportance to him. I worked with him in intimate collaboration for some 26 years at Paddington Green and Willesden, and I cannot remember that we were ever at variance. I always trusted him absolutely and grew to love him dearly.

Apart from his kindness and goodness, he had a well-ordered intellect and very shrewd and quick judgment. I think this explains why he was such a good committee man and chairman. His sound common sense and honesty of purpose were a great source of strength to any organization with which he was connected. One of the things about Pearse Williams which impressed me more than any other of his attributes was his cheerfulness and humour. I remember so many little leg-pulls given with a twinkle in his eyes. This is the more remarkable in that he had many sorrows and disappointments to bear, the chronic invalidism of his first wife and the untimely death of his only son, Raymond, in his seventh year, from acute osteomyelitis in Paddington Green. In 1957 he was struck down with a hemiplegia. He fought hard against this, and in fact did return to work for a short time, but recovery was not to be. I think, however, that he felt happy that his last days were spent in the hospital he loved so much.

J. B. COOK, M.D., D.P.H.

Dr. J. B. Cook, honorary consulting physician to the West Middlesex Hospital, of which he had formerly been medical superintendent, died at his home in Richmond, Surrey, on February 8, aged 81.

Joseph Basil Cook, who was born on October 26, 1877, received his medical education at Owens College, Manchester, and St. Bartholomew's Hospital. Graduating M.B., Ch.B. from the Victoria University of Manchester in 1902, he proceeded M.D. two years later, and he took the D.P.H. of Cambridge in 1907 before he decided to make hospital administration his career. After graduation he held resident appointments at the Royal Alexandra Hospital for Children at Brighton and at the Kensington Infirmary. Later he became medical superintendent at St. Giles Infirmary, Bloomsbury. In November, 1913, he was appointed medical superintendent of the West Middlesex Hospital (then known as the Isleworth Infirmary), and he early made his mark on the hospital which he was to serve until December, 1945. During the first world war he volunteered for service in the R.A.M.C. and was in France for much of the war. He returned to his hospital after the war, and saw many changes during the ensuing years.

An active member of the Medical Superintendents' Society, he was its president in 1932. He was also an ex-president of the Hunterian Society, and at one time he served on a number of B.M.A. committees, including the Hospitals Committee.

Dr. MARJORY W. WARREN writes: Dr. J. B. Cook fully earned his reputation as one of the great hospital administrators of his era. Throughout a difficult but most interesting period—from 1913 to 1945—he did a great deal to improve the standard of care and treatment of patients in his hospital. His success was due to his progressive hospital planning—he was no mean architect and was quite a medical authority on the subject between the wars—and his wide clinical interest. But perhaps more than to these qualities his success was due to his innate knowledge of good human relationships, his sagacity, his wisdom, and his superb, almost boyish, sense of humour.

Those of us who had the privilege of working under him recognized in him a strict disciplinarian and one who expected a high standard in others. Throughout the war he undertook himself a major share of those irksome extra war-time duties and was a continuous example to all of us with his unfailing sense of duty. He showed a personal interest in the welfare and happiness of his staff, but the comfort and care of the patient was always his first concern. He had a perfect sense of fairness and was a great advocate of personal freedom. Many in the medical and nursing profession must remember with gratitude help and advice given by him on a personal and on a professional level, and his lasting contacts with so many of those who had worked with him is ample testimony of the affection with which his staff regarded him. He had a large circle of friends.

He was a keen and very knowledgeable angler and gardener, and had in addition many interests and hobbies, including stamp collecting, church architecture, and photography. He travelled extensively in Europe and was keenly interested in international affairs. His death came after a long and trying illness, during which his wife was his constant companion.

MUNGO PARK, M.B., Ch.B.

Dr. Mungo Park, who had been in general practice at Harrow for some 30 years, died at Harrow Hospital on February 12. He was 55 years of age.

Mungo Park was born on July 20, 1903, and was educated at Edinburgh University, where he graduated M.B., Ch.B. in 1925. In those days he was a distinguished golfer. He came to Harrow in 1926 and remained there until his death.

J. W. S. writes: When he came to Harrow 30 years ago Mungo Park quickly built up a large practice in a newly developing part of the district. He soon became known for his great courtesy, sound judgment, and high ethical sense, and he showed great skill as a domiciliary obstetrician when called in for emergency work by the local midwives. He was devoted to the idea of the general-practitioner hospital, and served Harrow Hospital successively as an honorary member of the medical staff, as a duty medical officer, and finally as a very efficient and well-liked chairman of the medical committee. He also took an active part in the affairs of the St. John Ambulance Brigade for many years. In 1939 as a Territorial officer he was called up at once, and continued to devote his usual energy to military duties. He served in England and, later, in the Burma campaign, and retired with the rank of major.

He came back to Harrow to a depleted practice, but, accepting the position with his usual philosophic calm, proceeded to build up again one of the largest practices in the district. He also found time to be the captain of Grimsdyke golf club, where he was universally liked and respected. In my younger days I had reason to be grateful to him on many occasions of difficulty, and to me he was something of an elder brother. I owe more to him than he ever knew. He leaves a widow, who, too, was devoted to the welfare of Harrow. His only daughter, Dr. Sheila Baird, also graduated in Edinburgh and is now living there. Mungo Park was one of the old school, and we all mourn his loss. Medical practice in Harrow is very much the poorer for his going.

Medical Notes in Parliament

CHIROPODY SERVICE

The MINISTER OF HEALTH announced on March 2 that he was now ready to approve proposals by local health authorities who wished to provide a chiropody service as part of their arrangements for the prevention of illness under Section 28 of the National Health Service Act. He proposed to consult the local authority associations immediately on the terms of a circular to be sent to the authorities. He added in response to several questions that he intended to ask the authorities to give priority in the early years of the new service to the elderly, the physically handicapped, and expectant mothers. He would expect it to be based on a clinical approach. It was difficult to estimate the cost; on a national basis it could be expected to rise to between £1m. and £2m. over the next few years. Chiropodists employed by local authorities would have to possess one or other of the qualifications prescribed under the Health Service medical auxiliary regulations.

In reply to a question asking about the registration of chiropodists and the use of fully qualified chiropodists in a national chiropody service for old people, Mr. WALKER-SMITH said he had in draft a scheme for the registration of medical auxiliaries—which included the registration of chiropodists—on which he was further consulting the medical profession. Meanwhile the qualifications of chiropodists employed in the Health Service were governed by statutory regulations.

HOSPITAL WAITING-LISTS

Several M.P.s representing constituencies in the north-east used the opportunity of an adjunct debate on February 23 to discuss the problem of hospital waiting-lists in the area covered by the Newcastle Regional Hospital Board. The case, as presented by Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.), was, first, of the waiting-list for consultant appointments, on which general practitioners had complained to the Northumberland executive council; and, secondly, of the waiting-list for beds.

Six Weeks for a Consultation

Some waiting-lists for consultant appointments were as long as five or six weeks, and it was felt by the public that one of the most reliable ways of securing an early consultation was by paying for it. A wider provision for consultant and specialist services might lead to a considerable reduction in the waiting period, and consequently to some reduction in the number of people who tried the short cut of private consultation. The waiting period for beds, after some years in which there had been reductions, had in the past two years suffered a reverse. This, he suggested, was related in part to the Government's refusal to permit effective expansion of the specialist services. The increase had been most noticeable in general surgery, gynaecology, and orthopaedic treatment. The regional board's report showed that there were 9.5 beds per 1,000 population, against a national average of 11.6.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) complained that members from this and other areas had been questioning the Minister repeatedly on this subject, but had received only evasive answers and sympathy, and nothing had been done. She had been told on one occasion that many of the people were suffering from a chronic condition, the implication being that it did not matter that they had to wait. It was being said too often that admission could be expedited by payment of a fee.

Virtually the National Average

Mr. RICHARD THOMPSON, Parliamentary Secretary, Ministry of Health, said that the total number of patients waiting in the area, in relation to hospital facilities, was virtually identical with the national average. The number of specialists in the area was increased from 164 to 409 between 1948 and 1957. It tapered off in the latter part of the period, but the Minister was always prepared to look at proposals from the regional board and give them most careful consideration. The Newcastle region entered the Health Service relatively handicapped because its hospital facilities were limited and sometimes below acceptable standards. Allowance had been made for this in the distribution of capital, and the region had always had more than its share, reckoned on a strict population basis. Including the two new schemes announced in December, nine building schemes to the value of £11m. had been contained in the centrally financed programme, including one at the Newcastle teaching hospital. A sum of £8½m. had already been spent in the region since 1948, and the waiting-list had been reduced from its peak of 32,000 in 1953 to about 27,300 at the end of 1958. As these new facilities came into operation, he felt the picture would progressively improve.

Pay Beds and Private Patients

There was no substance in the argument that waiting-lists could be reduced if all pay beds were transferred to the Health Service use. On average, 70% were occupied, and half the patients were Health Service cases admitted as urgent or for special medical reasons. The total number of unoccupied beds involved was between 60 and 70, for a population of three million for whom over 27,500 Health Service beds were available.

MENTAL HEALTH BILL

The House of Commons committee which has the Mental Health Bill under examination (see *Journal*, February 28, p. 592) was embarked on the compulsory detention clauses after two further meetings on February 24 and 26, and had come upon a clear division of opinion on the purpose of the proposed review tribunals.

Compulsory Observation

On Clause 25, which sets out the procedure for admission to hospital for observation, Dr. DONALD JOHNSON (Carlisle, Con.) had the support of Dr. EDITH SUMMERSKILL (Warrington, Lab.), Mr. SOMERVILLE HASTINGS (Barking, Lab.), and Dr. A. D. D. BROUGHTON (Batley and Morley, Lab.) in objecting to the word "expedient" in section 1(b) in the context that an application for admission might be made because it was "expedient" in the interests of the patient or for the protection of other persons that the patient should be so detained. The case against it was that it tended to mean that the action taken was not the best, that it could suggest an ulterior motive, and that it left loopholes for abuse.

The MINISTER OF HEALTH pointed out the different phraseology used in the clause relating to observation, where the word was "expedient," and in that relating to treatment, where "necessary" was used—a difference arising from the different circumstances investing observation and treatment. To use "necessary" at the observation stage would be to ask for a degree of certainty which would then be premature. He accepted that "expedient" had suffered a degeneration of meaning, thought that "desirable" might suit, and promised to find a better word at a later stage of the Bill.

Sir HUGH LUCAS-TOOTH (Hendon, South, Con.) took exception to the phrase "in the interests of the patient," on the ground that it was too wide. He sought to make it read "in the interests of the patient's health or safety." He wanted to be sure that the grounds of detention were broadly medical, and that a person was not compelled to enter a hospital because, for example, he was a spendthrift.

Mr. WALKER-SMITH quickly accepted the amendment. He agreed with the desire that these provisions should be drafted as tightly as possible. The patient's need for treatment was one reason for the exercise of compulsory powers, but he was anxious that they should not go beyond matters of health and safety.

New Subsection to the Clause

Dr. EDITH SUMMERSKILL also had an amendment to this clause accepted. This was a new subsection (4), providing that nothing in the clause should preclude a patient admitted for observation from receiving such treatment as the responsible medical officer considered appropriate. She said that she had discussed this with psychiatrists, and had been impressed with their conclusion that within a month [the observation period is 28 days] there could often be a remarkable improvement in the patient if the appropriate treatment was administered. As the Bill stood, no treatment could start until the admission formalities were completed.

Mr. WALKER-SMITH agreed; indeed, one purpose of observation might be to see how the patient responded initially to treatment. The amendment was agreed to.

Admission for Treatment

On Clause 26 (admission for treatment) the Minister accepted as useful an amendment moved by Mr. K. ROBINSON (St. Pancras, North, Lab.) to insert the word "medical" in section 1(a)(ii), so providing that an application for admission might be made on the ground that the patient was suffering from mental disorder "of a nature or degree which renders him suitable to be detained in a hospital for *medical* treatment." The Minister undertook to make complementary amendments in Clauses 59 and 71, and possibly others.

Dr. DONALD JOHNSON introduced a new subsection (5), requiring that "all applications for admission for treatment shall be lodged with the Mental Health Review Tribunal, which shall within 28 days either discharge the patient or authorize his detention. . . ."

Admission for treatment, he said, was in effect an indefinite order for detention, with the patient losing his liberty. Many doctors were extremely anxious about being asked to take away a patient's liberty and civic rights without the intervention of a civic authority. That was what the amendment provided for. The review tribunal would take responsibility for the detention, rather than the doctor. The tribunal would be better able to make an independent decision on the patient's rights, whether he should be treated or not, when it considered the matter afresh, rather than in considering an appeal against a decision already taken by doctors and put into force. He also believed they would get better people on the tribunals if they were given more responsibility in this way.

There was the danger of irresponsible action by doctors due to the pressure of relatives. There was also, from the patient's point of view, the medical enthusiasm for treatment which on occasion was apt rather to run riot. He had had many complaints from patients that they had been given treatment they were unwilling to have and did not like.

Dr. BROUGHTON supported the amendment. Mr. ROBINSON said its effect would be to turn the appeal tribunals into scrutiny tribunals, and would involve another tier to appeal to from their decisions.

Tribunals not for Scrutinizing Admissions

Mr. WALKER-SMITH advised the committee to reject the amendment. He regarded the tribunals as appeal tribunals, where the initiative was taken by the patient, and not as scrutiny or admission tribunals. The Royal Commission had said [in para. 442]: "We do not recommend that these tribunals should automatically review every case in which compulsory powers are used, nor that they should have a continuing power of discharge. Our recommendation is that patients . . . should have a right to apply to such a tribunal, if they so desire, on specific occasions." That was what the Bill was drafted to do, and the amendment contravened those principles, because it would impose this procedure on all patients alike. It would destroy the appeal tribunals, by bringing them in as scrutiny tribunals, and they would not be able to operate in the way they were designed to operate.

Dr. JOHNSON had the last word: they must agree to differ; he must press the amendment. The amendment was negatived.

QUESTIONS IN THE COMMONS

Private Patients in Hospital

Mr. SOMERVILLE HASTINGS asked on March 2 if the Minister would give the percentage of beds reserved for patients who paid for both accommodation and treatment in the hospitals under his direction in each of the last five years; and whether the percentage of empty places in such beds was greater or less than in those not so reserved. Mr. WALKER-SMITH said the proportion of hospital beds designated for private patients in each of the last five years for which figures were available slightly exceeded 1% of the whole: the percentage of empty places in such beds was greater than in others.

Mr. HASTINGS said there was an idea that pay beds, instead of being used by ordinary patients, were kept vacant for paying patients. Had the Minister any evidence whether that was the case? Mr. WALKER-SMITH: I have no evidence of that. Pay beds are available for Health Service patients who urgently require accommodation on medical grounds and for whom no other suitable accommodation is available.

Supply of Doctors

Mr. ROBINSON asked the Minister what steps he would take to ensure that sufficient doctors qualified in Great Britain or with some postgraduate training in Britain were available to fill outstanding vacancies up to and including registrar grade in the hospital service. Mr. WALKER-SMITH said he did not consider that special steps were needed. The number of doctors available for civilian employment would increase between now and 1962 as the number of medical officers needed by the armed Forces declined.

Mr. ROBINSON said that a hospital in Wales, for example, had been unable to recruit any British qualified doctor for any house-surgeon post, and a well-known London hospital was finding it impossible to fill an orthopaedic house-surgeon post. He thought more urgent action by the Minister was required. Mr. WALKER-SMITH replied that generally speaking the position was improving. There had been a substantial intake of hospital junior medical officers in the last two years, 1956–7, at appreciably more than the rate visualized as necessary by the Willink Committee.

Mr. A. BLENKINSOP asked for an assurance that the Minister was doing nothing to recommend the proposals of the Willink Committee for reducing the numbers entering medical training schools. Mr. WALKER-SMITH said he had defined the position in regard to the Willink Committee at the time they reported, and he was keeping an eye on these general trends. The intake had been higher than the committee visualized, and that, together with the increasing number becoming available from the Forces, should meet the question that Mr. Blenkinsop had in mind.

Tax Relief for Psychiatrists

Mr. ROBINSON asked the Chancellor of the Exchequer on February 24 why, under his regulations, when a psychiatrist underwent a training analysis for the purpose of increasing his therapeutic skill, no part of the cost of such an analysis was allowed by the Inland Revenue authorities as a deduction from income for income-tax purposes. Mr. HEATHCOAT AMORY replied that, if this question related to psychiatrists in salaried employment assessed under Schedule E, the cost of personal analysis was not regarded as satisfying the test laid down by law, which was that expenses were deductible only if incurred wholly, exclusively, and necessarily in the performance of the duties of the employment.

Mr. ROBINSON said that the purpose of this analysis was solely to make a man a better doctor. Many younger psychiatrists were spending as much as £500 a year—perhaps a third of their gross salary—on these courses in the interests of their patients. Would he discuss with the Minister of Health whether some steps could be taken towards remedying this gross injustice? Mr. AMORY replied that he did not disagree about the importance of the training, but the test under Schedule E was very strict, and these courses, deserving as they were, did not seem to amount to an essential qualification for employment.

Filter-tip Cigarettes

Mr. C. OSBORNE (Louth, Con.) asked the Minister of Health, in view of the fact that cigarette consumption in the United Kingdom rose by 2½% in 1957 to 102,288 millions and increased by another 3% in 1958, what new information he had to give on the effect of cigarette smoking on lung cancer; and to what extent official research proved that filter-tipped cigarettes were less dangerous.

Mr. WALKER-SMITH stated that no new information of major significance on the relationship between lung cancer and smoking had become available since the statement by the Medical Research Council in 1957; a number of subsequent papers and reports had, however, confirmed the Council's assessment. There had been no official research in this country to demonstrate whether filter-tipped cigarettes were less dangerous. It continued to be the Government's policy to make the risks of smoking known to the public through local health authorities as part of their health education measures.

Hazards of Diagnostic Radiology

Mr. SYDNEY IRVING (Dartford, Lab.) asked the Minister what steps were being taken to ensure that general practitioners and others were aware of the risks in diagnostic radiology; and when he expected to receive the report of Lord Adrian's committee on the hazards from radiation.

Mr. WALKER-SMITH, in a reply on February 24, stated that the Secretary of State for Scotland and he had just received an interim report from Lord Adrian's committee. The report would be published as soon as possible. It dealt mainly with mass miniature radiography, the value of which the committee considered far outweighed any effects of the very small amount of radiation involved. It also included some preliminary observations on radiological procedure generally, but comprehensive recommendations on this must await the completion of the detailed survey of present practice which the committee were making. Meanwhile the need to keep exposure to medical radiation to the minimum was well recognized by the medical profession.

Hospital Facilities for Sterilization

Mr. B. BRAINE (Essex, South-East, Con.) asked the Minister of Health what action he was taking with regard to the report of the operational research team of the Nuffield Provincial Hospitals Trust,* for whom he provided facilities, which revealed that the sterilizing techniques employed in the six hospitals covered by the team's inquiry were inadequate and that this was contributing to the present high incidence of hospital infection. Mr. WALKER-SMITH replied that the report had been widely publicized and was by now well known to hospital authorities. In addition, the attention of the senior administrative medical officers of regional hospital boards had been specifically drawn to it; and in allocating sums to those boards for their revenue expenditure in 1959–60 he had asked them to have regard to the report in determining their expenditure. He would similarly be drawing the attention of boards of governors of teaching hospitals to this matter within the next few days.

Anti-measles Vaccine

Mr. SYDNEY IRVING (Dartford, Lab.) asked the Minister what progress was being made with an anti-measles vaccine. Mr. WALKER-SMITH replied that, while he understood that progress had been made in the preparation of such a vaccine, he was not at present aware of any proposal to manufacture it for general use.

*See *Journal*, December 27, 1958, p. 1582.

Medico-Legal

THE FORGOTTEN SWAB

SURGEON'S SUCCESSFUL APPEAL

[FROM OUR LEGAL CORRESPONDENT]

Last June, in order to illustrate the principle that the surgeon's legal duty regarding the removal of swabs during operations is to take such care as would be expected of an ordinarily good and careful practitioner in the circumstances of the particular operation, we reported shortly a recent case in Nairobi in which Mr. Justice Miles awarded £2,809 damages against the surgeon and the hospital authority (*Journal*, June 14, 1958, p. 1425; August 16, p. 462).

A Life-saving Operation

In that case a married woman had been admitted to the New European Hospital, Nairobi, in a state of collapse from internal haemorrhage from a ruptured tubal pregnancy. After massive saline and plasma injections and blood transfusions she became "just an operation risk," but her condition was so critical that although she was taken to the operating theatre she was operated on in her bed. The surgeon, Mr. Gerald Nevill, found that the left-hand corner of the uterus had burst, seized and held the bleeding point to control further bleeding, and succeeded in sewing up the ruptured part.

A large number of mopping packs had to be used (in addition to suction into auto-transfusion bottles) to remove some 6 to 7 pints (3.4–4 litres) of blood from the abdominal cavity, and two or three restraining packs were also used.

Bleeding stopped within 30 seconds from the time Mr. Nevill found the bleeding point, and during the rest of the operation the patient's condition began slowly to improve. Mr. Nevill, after dealing with the bleeding point and checking that the pelvic cavity was clear of swabs, removed the packing swabs and checked the area involved, removing considerable quantities of blood still oozing from the upper part of the abdomen. When satisfied that he had carried out his routine check and when he had been told by the theatre sister that the swab count was correct he sewed up.

At a subsequent operation for intestinal obstruction the cause was found to be a swab, which the judge held was left in her abdomen during the emergency operation by Mr. Nevill, although the possibility that it had come from a previous operation was canvassed and rejected. He also decided that in addition to negligence by the theatre staff over the count Mr. Nevill himself must have been negligent in his check, and that by reason of the improvement in the patient's condition during the operation Mr. Nevill's own evidence had excluded the existence of conditions which might reasonably excuse a surgeon from overlooking a swab.

Mr. Nevill Exonerated

On November 24, 1958, the Court of Appeal for Eastern Africa gave judgment allowing Mr. Nevill's appeal and exonerating him from negligence. They confirmed the judge's finding that the swab which caused the intestinal obstruction had been left in the patient's abdomen during the operation performed by Mr. Nevill. They held, however, that the judge had failed entirely to appreciate that the patient was in a state of collapse during the whole of the operation, and the improvement in her condition which followed the arrest of the bleeding was simply that she was no longer actually dying but might possibly survive.

The evidence was that Mr. Nevill before sewing up had made both a visual and tactile search; that it would have been bad surgical practice and probably fatal to the patient to carry out a general search of the abdominal cavity; that he made and relied on his own mental count of the restraining packs and was under no duty to memorize the mopping packs; and that he relied on the theatre sister's count, and she was someone of whose efficiency he had good reason to be confident. Mr. Nevill had used due care and attention to avoid the mishap which occurred, and his search was as extensive as was proper in the circumstances.

Setting aside the judgment and decree against Mr. Nevill, the vice-president of the Court observed that it was somewhat ironic to consider that the patient had not been Mr. Nevill's patient before the emergency arose, that if he had declined to operate or had delayed operation in the hope that conditions might become easier she would probably have died, and that if she had died before, during, or shortly after the operation no word of criticism of his conduct would ever have been uttered.

Hospital Authority's Appeal Dismissed

The Court, however, dismissed the appeal of the hospital authority, though it reduced the general damages awarded to the patient from £2,500 to £750. The Court agreed that a miscount of the swabs had taken place, though not necessarily through negligence on the part of the theatre sister, since an extra pack might through a miscount have gone into the sterilizing drum and two old packs might have adhered to each other and looked like one new one. But theatre routine was designed to deal with emergency operations as calmly and efficiently as with cold operations, and a critical operation like this one, whatever the particular problems it imposed on the surgeon, did not necessarily disturb the routine of the theatre staff. The vice-president added that he was far from saying that a miscount could never occur without negligence. It might be explainable in all sorts of special ways, but no such explanation at all had been put forward in this case or could be suggested on the evidence, and so the hospital authority's appeal on liability was dismissed.

Vital Statistics

Influenza and Pneumonia

Deaths from influenza in England and Wales numbered 1,121 in the week ending February 21, compared with 455 in the previous week. 1,951 deaths from pneumonia were recorded, as compared with 1,373 in the previous week, and there were 2,339 notifications of pneumonia, compared with 1,465 in the previous week.

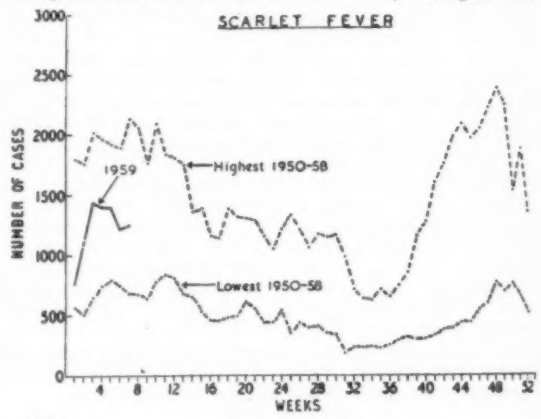
The age distribution of the influenza deaths was as follows: under 15 years, 24; 15–64, 329; 65 and over, 768. Deaths from influenza numbered 147 in London, 79 in Birmingham, 19 in Manchester, and 16 in Liverpool.

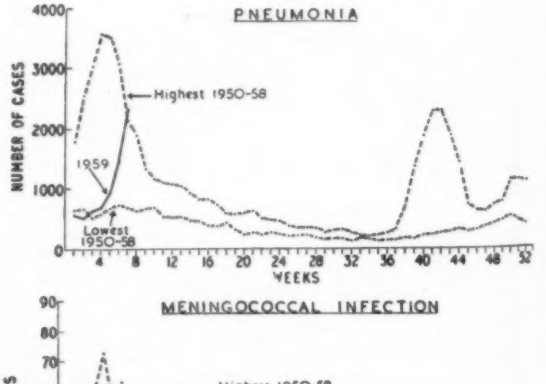
In the great towns of Scotland 27 deaths from influenza were recorded; in Northern Ireland none, and in Eire 3.

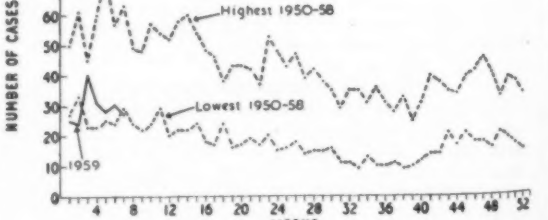
According to the Ministry of Health, the peak of the influenza outbreak may have been passed in some areas. Mortality is similar to that in 1953 and the autumn of 1957 (when the Asian virus first reached Britain).

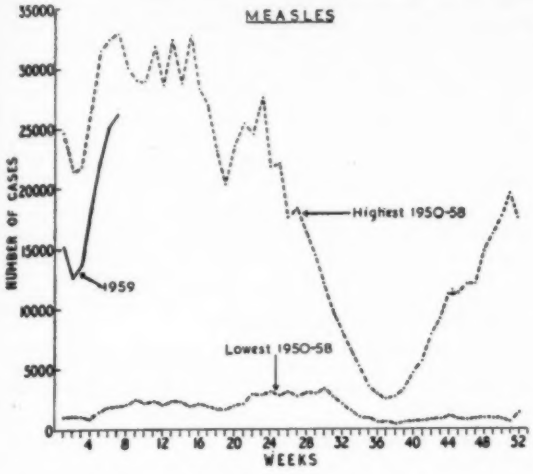
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ·-·-·-·, the figures for









1959 thus ———. Except for the curves showing notifications in 1959 the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

Week Ending February 21

The largest increases in the numbers of notifications of infectious diseases in England and Wales during the week ending January 10 were 1,307 for measles, from 25,157 to 26,464, 874 for acute pneumonia, from 1,465 to 2,339, and 27 for scarlet fever, from 1,218 to 1,245; the largest decreases were 213 for whooping-cough, from 788 to 575, and 153 for dysentery, from 1,346 to 1,193.

The largest rises in the incidence of measles were 201 in Durham, from 911 to 1,112, 175 in Gloucestershire, from 442 to 617, 168 in Northumberland, from 359 to 527, 161 in London, from 1,400 to 1,561, 160 in Hertfordshire, from 646 to 806, 152 in Cheshire, from 796 to 948, 111 in Essex, from 2,636 to 2,747, and the largest falls were 139 in Middlesex, from 1,714 to 1,575, 92 in Devonshire, from 341 to 249, 83 in Surrey, from 1,104 to 1,021. The largest rise in the notifications of scarlet fever was 26 in Yorkshire West Riding, from 111 to 137. The largest fall in the incidence of whooping-cough was 78 in Hertfordshire, from 81 to 3. Two cases of diphtheria were notified, being 3 fewer than in the preceding week.

The largest centres of dysentery were Lincolnshire 246 (Grimsby C.B. 106, Boston M.B. 50, Cleethorpes M.B., 28, Scunthorpe M.B. 25), Yorkshire West Riding 153 (Leeds C.B. 50, Bradford C.B. 37, Barnsley C.B. 18), Warwickshire 112 (Coventry C.B. 78, Birmingham C.B. 19), Glamorganshire 98 (Cardiff C.B. 51, Rhondda M.B. 28, Barry M.B. 11), Lancashire 95 (Manchester C.B. 42, Liverpool C.B. 14), London 78 (Wandsworth 16, Greenwich 15), Yorkshire East Riding 55 (Kingston upon Hull C.B. 49), Middlesex 42 (Tottenham M.B. 30), Northumberland 34 (Morpeth R.D. 12), Essex 24 (West Ham C.B. 10), Nottinghamshire 23 (Beeston and Stapleford U.D. 16), and Durham 21 (South Shields C.B. 11).

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in January was 82, compared with 107 in the previous month and 86 in January, 1958.

The numbers of cases of industrial diseases in the United Kingdom reported during January, 1959, were as follows: lead poisoning 5, anthrax 2, epitheliomatous ulceration 18, chrome ulceration 10; total 35. There were no deaths.—*Ministry of Labour Gazette*, February, 1959.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending February 14 (No. 6) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	5	0	4	0	2	3	0	4	0	4
Dysentery	1,346	88	97	37	7	1,060	182	196	13	2
Encephalitis, acute	3	0		0		3	0		0	
Enteric fever:										
Typhoid	2	0	1	0		2	0	0	0	
Paratyphoid	3	1	2(B)	0		2	0	0	0	12(B)
Food-poisoning	125	18	9	0		163	15	70	0	
Infective enteritis or diarrhoea under 2 years				12	21				6	29
Measles*	25,157	1400	594	406	1007	3,752	64	94	26	16
Meningococcal infection	30	5	9	0	1	37	6	13	0	
Ophthalmia neonatorum	24	1	7	0		26	0	7	0	
Pneumonia†	1,465	142	663	16	14	1,023	123	374	22	5
Poliomyelitis, acute:										
Paralytic	11	1	0	0		16	0	2	0	3
Non-paralytic	0	0	2			4	0			
Puerperal fever§	237	40	10	0	1	243	58	10	0	
Scarlet fever	1,218	60	64	27	29	871	67	68	23	24
Tuberculosis:										
Respiratory	457	55	75	15		599	64	105	16	
Non-respiratory	50	1	14	3		68	5	13	5	
Whooping-cough	788	26	54	90	140	721	38	26	5	21

DEATHS	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	1
Dysentery	3	0		0		2	0	0	0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	12	0	1	2	0	8	0	0	0	3
Influenza	455	44	29	1	0	184	13	2	0	2
Measles		0	1	0	0		0	0	0	0
Meningococcal infection		1	1				0	2		
Pneumonia	1,373	177	117	30	16	891	81	42	25	8
Poliomyelitis, acute	0	0		0	0	2	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	108	9	14	0	2	121	11	14	2	2
Non-respiratory		2	0	0	1		1	1	0	1
Whooping-cough	4	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	405	45	43	14	16	390	28	33	9	20
Deaths (excluding stillbirths)	15,007	1509	1146	169	228	12,631	976	717	155	221
LIVE BIRTHS	14,592	1243	1092	254	403	14,283	1151	954	221	393
STILLBIRTHS	310	20	23			350	29	34		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia

Medical News

Jerusalem Ophthalmic Hospital.—Work will begin on the main building of the new ophthalmic hospital of the Order of St. John of Jerusalem, Jordan, on March 5. Two foundation stones will be laid: one, inscribed in English, by the Chancellor of the Order of St. John, Sir HENRY POWNALL, and the other, inscribed in Arabic, by the Hospitaller, Sir STEWART DUKE-ELDER. The warden's house and nurses' quarters are already finished and it is expected that the main hospital building will be completed in the autumn of 1960. It is designed for 70 to 100 beds and a large out-patient clinic. The hospital's Research Institute was completed in 1956.

Francis Amory Prize.—Under the will of Francis Amory, of Boston, who died in 1912, the American Academy of Arts and Sciences is to award a septennial prize or prizes in 1962 for outstanding work in the field of diseases affecting the human reproductive organs, in particular those of men. The average value of previous awards has been $3,700. Nominations for prizemen are now invited "from people familiar with developments in the field," with the proviso that an important part of the nominee's work for the prize must have been done during the seven-year period ending November 10, 1961. The work may be instrumental technology, operative procedure, clinical or laboratory research, or a technical treatise. The closing date for nominations is January 1, 1962, and they should be sent to the Chairman, Amory Prize Committee, American Academy of Arts and Sciences, 280, Newton Street, Boston, 46, Mass.

Fall-out in Water.—There is a much lower concentration of radiostrontium and radiocaesium in drinking-water than in rain, according to a report published on February 25 by the Atomic Energy Authority (*A Preliminary Survey of Radiostrontium and Radiocaesium in Drinking Water in the United Kingdom*, H.M.S.O., 2s. 6d.). Water from 13 major undertakings in the United Kingdom, representing lake, river, and well supplies, was tested from September, 1957, to June, 1958. The mean concentration of Sr-90 in lake-derived supplies was about 15% and in river-derived supplies about 10% of that in rain. Cs-137 levels were in general much lower than those of Sr-90. Routine measurements of these isotopes in rain-water have been carried out in the United Kingdom since 1954, but this is the first systematic study of their penetration into drinking-water.

New Milk Regulations.—The new Milk and Dairies Regulations, which come into force on March 8, bring the earlier regulations into line with modern methods of milk production. Among the new provisions are ones requiring persons to wear clean and washable overalls and caps when engaged in milking cows or in handling milk in open containers. They must also keep open cuts and abrasions covered with a waterproof dressing, and refrain from spitting and the use of tobacco, including snuff.

Children's Painting Book.—In future children who have to go into the Westminster Children's Hospital will be given a painting book before they are admitted, showing pictures of ward routine with simple explanations written by a psychiatrist. Money to produce the book was collected by children belonging to the hospital's Santa Claus Club, a junior branch of the League of St. Nicholas. The organizers believe that, although similar schemes are well known in America, this is the first painting book to be issued by a hospital in this country.

Lord Stopford of Fallowfield, F.R.S., Vice-chancellor and professor of experimental neurology at the University of Manchester, will be introduced in the House of Lords on March 10. He was one of the first 14 people to be granted life peerages.

Mr. E. A. Nicoll, consultant adviser in rehabilitation to the Ministry of Health, is to give a course of lectures and demonstrations on orthopaedic surgery in Rio de Janeiro at the invitation of the Brazilian Government, and will later visit Uruguay under the auspices of the British Council.

Dr. E. E. Pochin, director of the department of clinical research at University College Hospital Medical School, London, is to lecture on radio-isotopes to Italian medical schools by arrangement with the British Council.

Dr. A. R. Mills, of Edinburgh University, is to take part, with members of the department of social anthropology, in a study of the effects of rapid urbanization in a new mining community in Sierra Leone. He is a lecturer in the Department of Public Health and Social Medicine, and the Social Sciences Research Centre.

R.C.S., Ireland.—Mr. R. VAUGHAN HUDSON delivered the sixth Abraham Colles postgraduate lecture on "Selective Surgery of the Thyroid Gland—Diagnosis and Procedure," on February 16.

"Family Doctor."—The March issue includes articles on corneal grafts by Mr. B. W. RYCROFT, on bronchitis by Dr. K. C. HUTCHIN, and an account of the Liverpool mass radiography campaign.

COMING EVENTS

Institute of Dermatology.—An exhibition on "Cutaneous Tuberculosis and Sarcoidosis," organized by Dr. P. D. SAMMON, will be held during the winter course from March 2 to 28 at St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London, W.C.2.

University of St. Andrews.—A course in anatomy and physiology (including biochemistry) will be held at St. Salvator's College, October, 1959, to March, 1960. Details from the Dean of the Faculty of Medicine, University of St. Andrews, Queen's College, Dundee. Applications by May 1.

B.B.C. Television.—March 10, 9.30 p.m.: "What Causes Allergy Illnesses?" (Eye on Research). March 12, 10.15 p.m.: "Battle for the Mind" (Lifeline). "They Made History," also on March 12, 8.15 p.m., will reconstruct the scene in the operating theatre of University College Hospital when in 1846 Robert Liston performed the first operation in Europe on an anaesthetized patient.

B.B.C. Radio: March 13, 6.45 p.m., Network Three: "The Electronic Eye," by Dr. Pieter Schagen, Ph.D. (Science Survey).

Association of Industrial Medical Officers.—85th Meeting, March 20 and 21, at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, and St. Thomas's Hospital, London, S.E.1. Details from the Association, 47, Lincoln's Inn Fields, London, W.C.2.

Faculty of Radiologists.—Courses for candidates for the D.M.R.D. and D.M.R.T. (R.C.P.Lond., R.C.S.Eng.) starting in October, 1959, are now being organized. Particulars may be obtained from the Assistant Director, British Postgraduate Medical Federation, 18, Guilford Street, London, W.C.1.

The Nutrition Society (Scottish Group).—A symposium on "Obesity" will be held in Glasgow on April 4. Those who are not already members of the Society are invited to write for details to Dr. J. DAVIDSON, The Rowett Research Institute, Bucksburn, Aberdeenshire.

Industrial Welfare Society.—A one-day industrial health conference will be held at the St. Enoch Hotel, Glasgow, on April 14. Details from I.W.S., 48, Bryanston Square, London, W.1.

Welsh National School of Medicine.—A postgraduate course for general medical practitioners will be held in Cardiff from April 27 to May 9. Details and application forms from the Secretary, 34, Newport Road, Cardiff.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Industrial Medicine.—Issued four times a year (£3 annually). The new issue (Vol. 16, No. 1) includes:

INDUSTRIAL HEALTH—MEETING THE CHALLENGE. A. Meiklejohn.
THE TOXICITY OF EPICHLORHYDRIN VAPOUR. J. C. Gage.
THE RESPONSE TO HEINZ BODIES IN THE RAT. Philip Rofe.
TOXIC SOLVENTS: A REVIEW. Ethel Browning.
INVESTIGATIONS CONCERNING THE PRE-RADIOLOGICAL STAGE OF SILICOSIS. C. Velican, G. Latis, M. Popa, Gr. Popa, and M. Steinbach.
THE DUST CONTENT OF THE LUNGS OF COAL WORKERS FROM CUMBERLAND. J. S. Faulds, E. J. King, and G. Nagelschmidt.
RESPIRATORY FUNCTION AND DISEASE AMONG WORKERS IN ALKALINE DUSTS. C. P. Chivers.
QUARRY BANK MILL: PART 2. THE MEDICAL SERVICE. Robert Murray.

British Heart Journal.—Issued quarterly (£3 annually). The new issue (Vol. 21, No. 1) includes:

ACETYLCHOLINE AND THE PULMONARY CIRCULATION IN MITRAL VALVULAR DISEASE. Bror Söderholm and Lars Werkö.
CONSTRICTIVE PERICARDITIS. T. M. D. Gimlette.
TOMOGRAPHY OF CALCIFIED AORTIC AND MITRAL VALVES. Paget Davies and N. L. Bucky.
ELECTROCARDIOGRAPHIC CHANGES DURING POSITIVE ACCELERATION. M. K. Browne and J. T. Fitzsimons.
OBSERVATIONS ON HYPOXIC PULMONARY HYPERTENSION. W. C. Boake, Raymond Daley, and I. K. R. McMillan.
THE INCIDENCE OF CONGENITAL HEART DISEASE IN CHILDREN BORN IN GOTHENBURG, 1941-1950. Lars-Erik Carlgren.
SOME POSSIBLE CAUSES OF CONGENITAL HEART MALFORMATION. G. E. H. Foxon.
THE GENETICS OF CONGENITAL HEART DISEASE AND SITUS INVERSUS IN SIBS. Maurice Campbell.
PRIMARY PULMONARY HYPERTENSION IN THREE SIBS. P. N. Coleman, A. W. B. Edmunds, and J. Tregillus.
POST-PARTUM HEART DISEASE. Aaron Burlamaqui Benchimol, Raymundo Dias Carneiro, and Paul Schlesinger.
CONGENITAL DIVERTICULUM OF THE LEFT VENTRICLE. J. B. Lowe, J. C. P. Williams, D. Robb, and D. Cole.
A STABLE CUVETTE OF HIGH SENSITIVITY FOR INDICATOR DILUTION CURVES. John Norman.
THE EFFECT OF THYROTOXICOSIS ON THE ELECTROCARDIOGRAM. Gerald Sandler.
THE MYOCARDIAL FACTOR IN MITRAL VALVE DISEASE. H. A. Fleming and PAUL WOOD.
TRICUSPID INCOMPETENCE FOLLOWING SUCCESSFUL MITRAL VALVOTOMY. Patrick Mounsey.
POLYTHELIA IN CARDIO-ARTERIAL DISEASE. William Evans.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 9

GUY'S HOSPITAL.—5.15 p.m., Endocrine demonstration by Professor J. Butterfield and Dr. J. H. Briggs: Carbohydrate Metabolism.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Professor W. B. Shelley: Studies in the Nature of Itching.
LONDON UNIVERSITY.—At Physiology Lecture Theatre, University College, 5.15 p.m., special university lecture in biochemistry by Professor J. Folch-Pi (Harvard): Brain Lipoproteins and Proteolipids.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Guest lecture by Dr. Brian Ackner: Psychopathic Personality.

Tuesday, March 10

BELMONT HOSPITAL CLINICAL SOCIETY.—5.30 p.m., Professor Russell Fraser: Thyroid Disorders Presenting as Neurotic Disorders. Discussion to be opened by Dr. J. C. Batt.
BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Dr. M. Sim: Some Aspects of American Psychiatry.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor G. H. Lathe: Metabolism of Bilirubin.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. M. Feiwel: Skin Manifestations of Some Metabolic Diseases.
MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Clinical Sciences Building, 8 p.m., symposium by Mr. W. J. Metcalfe, Mr. F. S. Mitchell-Heggs, Mr. J. P. Lythgoe, and Mr. H. Haxton: Suturing of the Abdominal Wall.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Oliver-Sharpey Lecture by Dr. P. L. Mollison: Blood-group Antibodies and Red-cell Desruction.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Imperial Cancer Research Fund lecture by Mr. P. C. Williams: Hormones and Cancer.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Dr. P. E. Hughesdon: Pathogenesis of Endometriosis.

Wednesday, March 11

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. G. N. Jenkins: Biochemical Background to the Action of Fluoride in Dental Caries.
CHRISTIAN MEDICAL FELLOWSHIP.—At Royal Commonwealth Society, Northumberland Avenue, W.C., 8.15 p.m., Dr. D. Martyn Lloyd-Jones: Battle for the Mind.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Specific and Foreign Body Granulomata.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Professor D. W. Smithers: Oesophageal Cancer.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor E. Kugelberg (Stockholm): Nociceptive Reflexes in Man.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. K. Owen: Hypertension and the Kidneys.
LONDON UNIVERSITY.—At Physiology Lecture Theatre, University College, 5.15 p.m., special university lecture in biochemistry by Professor J. Folch-Pi (Harvard): Brain Lipoproteins and Proteolipids.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University, 5 p.m., Dr. S. Sevitt: Renal Failure and Tubular Necrosis in Burned and Other Patients.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. Betty Hobbs: Current Problems in the Control of Food-poisoning.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Philip Ellman: Social Implications of Chronic Bronchitis (illustrated).
ROYAL SOCIETY OF HEALTH.—2.30 p.m., Dr. L. G. Norman: Health of London's Travelling Public.

Thursday, March 12

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. C. L. Cope: Measurement of Adrenal Activity in Man.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Control of Fungous Infections.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., joint meeting with Liverpool Society of Anaesthetists. Discussion: Recovery Wards. To be opened by Dr. R. M. Danes.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8 for 8.30 p.m., annual general meeting. President's Address: Transatlantic Impressions (illustrated by slides).
MIDLAND THORACIC SOCIETY.—At Birmingham Medical Institute, 7.30 p.m., Dr. J. F. Bromley: Non-surgical Treatment of Intrathoracic Malignant Disease.
● NEW HEALTH SOCIETY.—At Board Room, Y.W.C.A. Central Club, Great Russell Street, London, W.C., 3 p.m., Dr. A. J. Dalzell-Ward: Health Education.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Oliver-Sharpey lecture by Dr. P. L. Mollison: Blood-group Antibodies and Red-cell Destruction.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor Alan Parks: Micro-anatomy of the Breast.
ST. ANDREWS UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor A. Bradford Hill, F.R.S.: Observation and Experiment in Medicine.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. J. Hamilton Paterson: neurology.
WESTMINSTER HOSPITAL MEDICAL SCHOOL.—5.30 p.m., clinico-pathological conference. A Case of Shortness of Breath.
WEST OF ENGLAND CHILD HEALTH GROUP.—At Department of Child Health Lecture Theatre, Children's Hospital, Bristol, 8.30 p.m., Dr. Philip Evans: Baby Farming.

Friday, March 13

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. F. R. Bettley.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., clinical lecture by Mr. Charles Heanley: Plastic Surgery of the Nose.
KEIGHLEY AND DISTRICT MEDICAL SOCIETY.—At Victoria Hospital, Keighley, 8.30 p.m., Presidential Address by Dr. W. Sefton Suffern: Recent Advances in Therapy.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. W. R. Henderson: Spinal Tumours. 4 p.m., Professor J. D. Hay: Pulmonary Stenosis in Childhood.
SOCIETY OF MEDICAL OFFICERS OF HEALTH: HOME COUNTIES BRANCH.—At London School of Hygiene and Tropical Medicine, 3 p.m., Dr. P. Hugh-Jones: Use of Lung Function Tests in Clinical Medicine.

Saturday, March 14

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Addenbrooke's Hospital, Cambridge, Symposium on Cardiovascular Diseases. Morning, 10.30 a.m., Mr. C. Parish: Surgery of Valvular Disease of the Heart; 11.30 a.m., Mr. B. B. Milstein: Surgery of the Arteries; 12.15 p.m., Dr. D. McC. Gregg: Radiographic Techniques in Cardiac Surgical Diagnosis. Afternoon, 2.30 p.m., (1) Demonstration of Clinical Cases: (*a*) Pre-operative; (*b*) Post-operative. (2) Dr. A. M. Barrett and the Staff of the Department of Pathology: Pathological Demonstrations of Heart Disease; 3.45 p.m., Dr. L. B. Cole: Anginal Pain; 4.30 p.m., "Any Questions?"
● FELLOWSHIP OF POSTGRADUATE MEDICINE.—At Rheumatism Unit, St. Stephen's Hospital, Fulham Road, London, S.W., 10 a.m., concentrated week-end course in the "Rheumatic Diseases."

Sunday, March 15

● FELLOWSHIP OF POSTGRADUATE MEDICINE.—At Rheumatism Unit, St. Stephen's Hospital, Fulham Road, London, S.W., 10 a.m., concentrated week-end course in the "Rheumatic Diseases."
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—10.15 a.m. to 12.30 p.m., seminar for general practitioners. Mr. Maxwell Ellis: Common E.N.T. Conditions.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Blackadder.—On February 21, 1959, at Edinburgh, to Jean, wife of Dr. Eric S. Blackadder, of 29, Grange Loan, Edinburgh, a sister for Mark and John.
Hewitt.—On February 21, 1959, at Plymouth, to Myrna (formerly Russell), wife of Stanley R. Hewitt, M.R.C.O.G., a son.
Sayers.—On February 11, 1959, at Brighton, Sussex, to Mary Marguerite (formerly Hay), L.R.C.P.&S.Ed., wife of W. J. Hastings Sayers, L.R.C.P.&S.Ed., a son—Jonathan Richard Hastings.

DEATHS

Bennie.—On February 4, 1959, at Paisley, Renfrewshire, Janet Bennie (formerly Todd), M.B., Ch.B., F.F.A.R.C.S., of 88, Renfrew Road, Paisley.
Dryerre.—On February 5, 1959, at the Royal Infirmary, Edinburgh, Henry Dryerre, Ph.D., M.R.C.S., L.R.C.P., of Kenmore, Broomieknowe, Lasswade, Midlothian.
Nicholls.—On March 1, 1959, at Royal Naval Hospital, Haslar, Hants, Surgeon Vice-Admiral Sir Percival Thomas Nicholls, K.C.B., F.R.C.S.Ed., of Oakapple Cottage, Emsworth, Hants, aged 81.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Poliomyelitis Immunization in Infancy

Q.—*What is the youngest age at which vaccination against poliomyelitis should be carried out, and why? Is there any reason why it should not be given first, thus reducing the risks of paralysis otherwise inherent in triple antigen (pertussis, diphtheria, and tetanus)?*

A.—The response of a newborn infant to poliomyelitis vaccine depends chiefly on the level of the placentally transmitted antibodies in its blood. According to the work of Perkins, Yetts, and Gaisford,[1] some 62% of newborn infants in England possess antibodies to all three types of polio virus, the level of each type being similar in mother and infant. Infants who have no maternal antibodies respond to poliomyelitis vaccine, though not equally well to each type; in those who have maternal antibodies, the antibodies interfere with the antigenic action of the vaccine. The same workers estimate that by the sixth to the ninth month the maternal antibodies will have either disappeared or fallen to non-inhibitory levels. It follows, therefore, that, in England at any rate, the earliest age for successful active immunization against poliomyelitis is the sixth month.

If all newborn infants were given a course of poliomyelitis vaccine soon after birth, those with a passive immunity from maternal antibodies—an increasing number with the present campaign against poliomyelitis—would receive at the best a basic immunity; completion of their immunization would still have to be done after 6 months of age. They could be given triple antigen without fear of provoking poliomyelitis, provided the injections were completed before the sixth month. In the case of those without maternal passive immunity, it would be uncertain to what extent they would be protected against the same risks, since two injections of poliomyelitis vaccine do not immunize more than 75% of all subjects. To get round the difficulty, it has been suggested—and this suggestion is being carried out in some places—that every pregnant woman should be immunized against poliomyelitis so that her infant would have at least four months of passive immunity during which immunization with combined antigens could be carried out.

REFERENCE

1 Perkins, F. T., Yetts, R., and Gaisford, W., *Brit. med. J.*, 1958, 2, 68.

Age Limit for Poliomyelitis Immunization

Q.—*What is the upper age limit for giving poliomyelitis vaccination?*

A.—No upper limit of age can be fixed for poliomyelitis vaccination. Some severe paralytic cases have been seen recently in Great Britain aged 60 to 75 years.

Migraine in Pregnancy

Q.—*What is the treatment of migraine in pregnancy, and are ergot preparations contraindicated?*

A.—Troublesome headaches, migrainous or otherwise, are not uncommon in pregnancy and their cause is generally unknown. Usually they have no demonstrable basis by way of a cerebral lesion, a defect in hearing or vision, anaemia and the like, but such possibilities need to be excluded. Empirical treatment includes ensuring that the patient takes proper amounts of exercise and rest, and that she avoids nervous exhaustion and smoking. Restriction of the intake of fluid and sodium sometimes appears to lessen the number of attacks. Calcium gluconate, 30 to 50 gr. daily, is occasionally advised, but the rationale is uncertain. Claims are also made for the efficacy of chlorpromazine, especially if the headache is accompanied by vomiting.

One of the most successful remedies for migraine is "cafergot," supplied in tablets each containing 1 mg. ergotamine tartrate and 100 mg. caffeine (alkaloid). The recommended dose is two tablets as early in the attack as possible, with a third and a fourth tablet at half-hourly intervals if necessary. However, there are over 40 cases in the literature in which ergotamine has caused effects on the capillary circulation which have gone as far as gangrene. It is therefore unwise to recommend the use of such large doses of ergotamine in pregnancy. Dihydroergotamine has a good deal of the action of ergotamine, and has not been found to cause gangrene. Still safer is ergometrine, though it is to be said that the proportion of patients with migraine who are relieved by ergometrine is less.

Nausea Before Jaundice

Q.—*What is the cause of the nausea in the pre-icteric stage of infective hepatitis, and why does it usually go with the development of the jaundice?*

A.—Nausea and vomiting are probably due to the initial invasion of the body, and particularly the liver, by the virus of infective hepatitis. Other symptoms such as fever, general malaise, headache, muscle and joint pains, anorexia and rashes, may also be present, and at this stage the disease may be indistinguishable from any other virus infection. If such an explanation is correct their disappearance with the onset of jaundice is simply owing to the fact that the prodromal stage of virus invasion is over.

Tubercle Bacilli in Dairy Products

Q.—*Are butter and cheese made of pasteurized milk? Is there any risk of children contracting bovine tuberculosis from these products, particularly imported cheeses?*

A.—All imported and almost all English butter is made from pasteurized milk. The same is true of cheese made on a factory scale, and in this there is the additional safeguard that tubercle bacilli die out in cheese during any prolonged ripening process. Mature Cheddar cheese can therefore not contain living tubercle bacilli whatever its origin. The only products of this kind which need cause any apprehension are farm butter and soft cheeses made on farms or in small dairies and eaten within a short time of making.

Correction.—There was a misprint in the answer to the question on eyes and furnace radiation ("Any Questions?" February 28, p. 598). In the sentence "Similar findings were reported from glass works where the maximum energy flux was 0.38 cals./cm.^{2}/sec." the maximum energy flux should have read "0.038 cals./cm.^{2}/sec"

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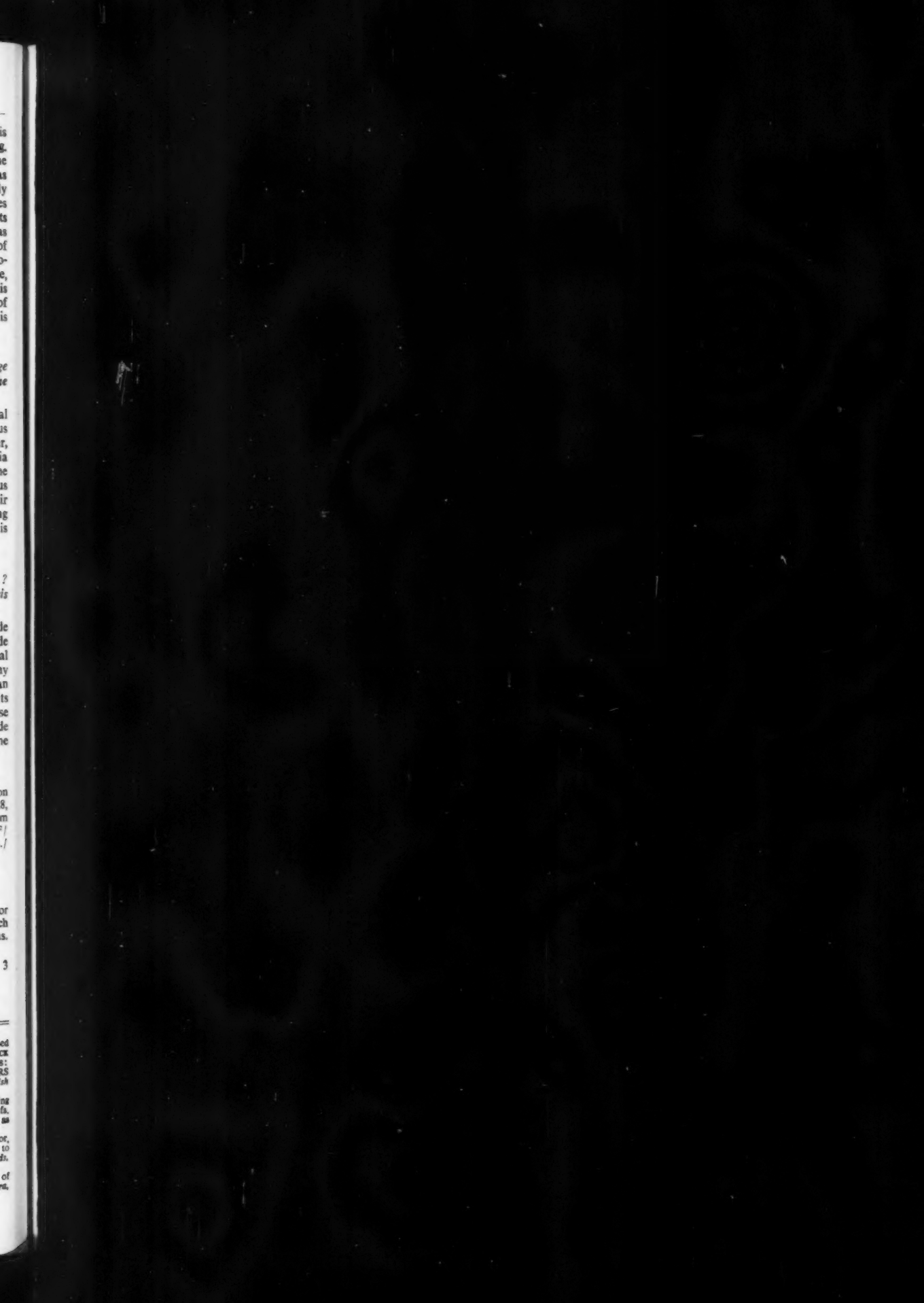
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